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THE SURGICAL TREATMENT OF URINARY INCONTINENCE*

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THE subject of exertional incontinence in women — or "stress incontinence," as it is frequently called — has stimulated the imagination of the medical profession for many years. Numerous operative procedures have been devised for the cure of this condition, but as yet no entirely satisfactory technic is available.

This study was stimulated by the work of Dr. William T. Kennedy,[1-3] of New York. His results were so far superior to those previously attained that they could not fail to arouse interest.

Up to the time this study was undertaken, the usual procedure employed at the Massachusetts General Hospital for the correction of exertional urinary incontinence was by means of a repair of the anterior vaginal wall and a figure-of-eight or mattress stitch placed at the bladder neck, after the method advocated by Kelly[4] in 1914. Discarding the untraced cases, Kelly's report showed 41 per cent cures. Our experience with this method gives essentially similar results. Cure may be expected in about half the patients on whom it is used. This is far from satisfactory, and in the uncured group the result is most disappointing to both patient and surgeon.

MECHANISM OF URINARY CONTROL

Much work has been done to determine the exact mechanism of urinary control in women. Careful and detailed anatomic study has been devoted to this subject, and excellent presentations by Kennedy,[2, 3] Davies[5] and Curtis[6, 7] have appeared in recent years. From this mass of detailed work, certain fundamental facts appear that may be used as a basis for an understanding of the problem of urinary incontinence.

The wall of the urethra contains involuntary muscle fibers that become more numerous in the region of the bladder neck, where they are arranged in a circular manner and form what is called the internal sphincter. This mechanism is under autonomic control and under normal conditions serves to maintain closure of the bladder outlet.

There is also a voluntary sphincter mechanism, which consists chiefly of the sphincter urethrae membranacea. This muscle is contained between the two fascial layers of the urogenital diaphragm, which bridges the anterior portion of the pelvic outlet running from one ischiopubic ramus to the other. The fibers of the sphincter urethrae membranacea arise from the inner surface of the inferior pubic ramus and from the investing fascial layers and encircle the urethra. Posteriorly, they blend with the deep transverse perineal muscle to encircle the vagina. The sphincter urethrae membranacea is innervated by the perineal branch of the pudendal nerve, and its action is to constrict the urethra, making possible the voluntary interruption of the urinary stream.

The anterior fibers of the levator ani arise from the inner surface of the superior ramus of the pubis, and as they run posteriorly to insert into the coccyx, a few fibers are given off to the urethra. The importance of these fibers in contributing to the voluntary sphincter mechanism has been stressed by some authors.

If the mucous membrane is elevated from the anterior vaginal wall and care is exercised to keep the dissection close to the mucosa, an avascular plane is encountered, and a firm fibrous layer is uncovered. This is the pelvic fascia, and as the dissection is carried forward toward the external meatus, the region of the urogenital diaphragm is exposed (Fig. 2).

MECHANISM OF URINARY INCONTINENCE

When a patient with stress incontinence is examined in the lithotomy position, the urethra, instead of pointing almost horizontally, usually assumes a nearly vertical direction. This sagging of the urethra and bladder neck away from the pubic arch, which was emphasized by Watson[8] in 1924, results from a tearing of the layers of pelvic fascia between the bladder and the anterior vaginal wall

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and the structures of the urogenital diaphragm. The displacement of the bladder neck and urethra impairs the function of the sphincter mechanism, leading to stress incontinence.

Whether the functional impairment of the sphincter mechanism is due to actual muscular damage to the sphincter urethrae membranacea or to loss of fixation of the urethra and its descent from a normal position behind the pubic arch has not been established.

FIGURE 1.

An incision has been made in the anterior vaginal wall. The bulging of the anterior vaginal wall proximal to the external meatus is due to the sagging of the urethra and bladder neck.

Under normal conditions the sphincter urethrae membranacea serves to allow voluntary interruption of the urinary stream. Its action is not normally required to prevent the involuntary escape of urine from the bladder even under conditions of stress and increased intravesical pressure. This function is fulfilled by the involuntary sphincter mechanism. It is my belief that stress incontinence occurs when the bladder neck and urethra sag away from their normal positions behind the pubic arch, because this results in a stretching and distortion of the bladder neck and proximal urethra that render ineffective the action of the internal (involuntary) sphincter.

The success of an operative procedure for stress incontinence depends on the replacement of the urethra and bladder neck in their normal positions, by whatever means attained, rather than on the reapproximation of voluntary muscle fibers. The importance of this restoration of normal anatomic relations in providing a good functional result has been emphasized by Kennedy.[9]

METHODS OF REPAIR

A great many surgical procedures have been devised for the cure of exertional urinary incontinence in women. They fall into three general types.

The first comprises attempts to reconstruct the existing structures of the urethra or bladder neck, or both, by means of a vaginal plastic procedure. These vary from the simple Kelly[4] stitch described above, and many modifications thereof, to more elaborate operations, such as that described by Kennedy[1–3] and Frost.[10] Kennedy's technic is based on the concept that, in addition to the displacement of the urethra and bladder neck described above, the function of the voluntary sphincter has been impaired by the formation or scar-tissue bands between the urethra and the pubic rami laterally. To correct this, the vaginal mucosa is elevated from the bladder neck and posterior two thirds of the urethra, and the dissection carried laterally under the pubic rami until the urethra is entirely freed of its lateral attachments, including any post-traumatic scar tissue that may be present. The urethra is then plicated in the midline to restore the function of the voluntary sphincter. Kennedy obtained excellent results by this method, reporting 35 cases with cures in 32.

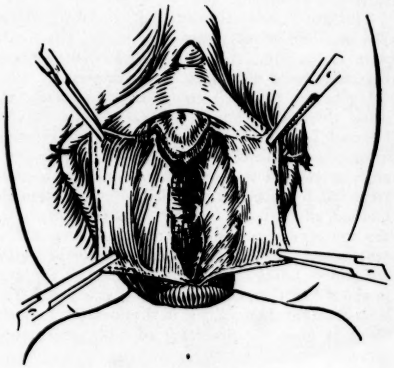

FIGURE 2.

The mucous membrane is elevated. In the midline the layers are adherent, and the cleavage plane is indistinct. As the dissection is carried laterally, close to the mucosa, a good avascular plane is encountered, which may be easily followed laterally to the pubic rami. The pelvic fascia is revealed as a smooth glistening layer, and as the dissection is carried anteriorly toward the external meatus, the region of the urogenital diaphragm is exposed.

The second general type of operative repair involves the use of various muscle or fascial transplants. Some of these procedures are done entirely from below, and others, partly vaginally and partly suprapubically. Portions of the levator muscles, the gracilis, the pyramidalis, strips of fascia from the rectus sheath or external oblique and various other

structures have been used. Recently, Price,[11] Aldridge,[12] Meigs[13] and Studdiford[14, 15] have reported excellent results through the use of a fascial sling.

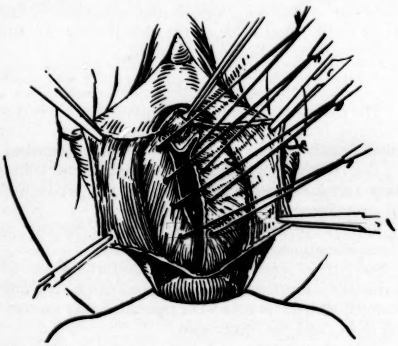

FIGURE 3.

The pelvic fascia and urogenital diaphragm are approximated over the urethra and bladder neck.

This method seems to offer a means of replacing the bladder neck in its normal position behind the pubic

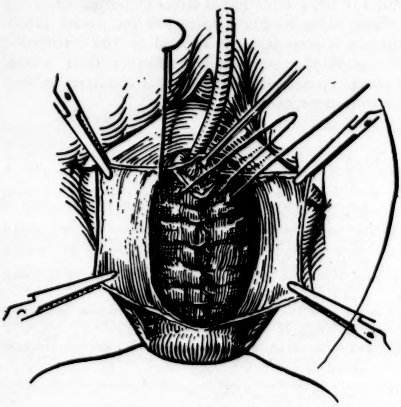

FIGURE 4.

The pelvic fascia and urogenital diaphragm are infolded by a second row of sutures.

arch when such replacement might be impossible to attain otherwise.

The third procedure employs the transvesical approach for the repair of the sphincter mechanism at the bladder neck. The value of recognizing the muscle of the trigone in the transvesical repair of the internal sphincter has been stressed by Macky.[16]

A nonoperative method for the treatment of stress incontinence was reported by Murless,[17] who employed periurethral injections of a sclerosing solution (5 per cent sodium morrhuate). By this technic he was able to produce cures in 60 per cent of a series of 20 cases.

MATERIAL STUDIED

In the selection of cases for this study, the choice was limited to patients in whom the condition was believed to result from the trauma of childbirth. Patients who were nulliparous or in whom some congenital abnormality was present were not included.

Sixty-three operations for the relief of stress incontinence were done on 62 patients. Of these, 15

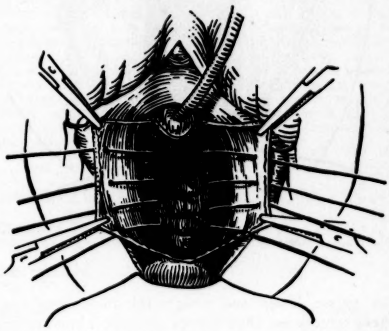

FIGURE 5.

Sutures are placed to close the mucous membrane and to anchor it to the underlying fascia. (This anchoring of the mucosa to the fascia has since been omitted.)

had had one or more previous operations for the same condition without success. These operations were done between 1939 and 1942, and it was believed that a follow-up study, after a period of over four years, would be of value. Of the cured patients, 12 could not be traced, and the follow-up period in these cases averaged fourteen months. The remaining 32 cured patients were traced, with an average follow-up interval of seventy months.

OPERATIVE PROCEDURE AND RESULTS

In the first 42 cases the technic described by Kennedy was followed as closely as possible. In this group 29 patients, or 69 per cent, were cured.

The stripping of the lateral attachments of the urethra from the pubic rami was then discontinued for two reasons: the dissection may result in considerable hemorrhage, from damage to the veins

about the bladder neck, which at times is difficult to control; and these lateral structures were considered to be the normal attachments of the pelvic fascia and urogenital diaphragm, so that their loss might interfere with the replacement of the bladder neck and urethra in the normal positions. Thus, in the last 21 cases the procedure resolved itself into the elevation of the vaginal mucosa from the entire urethra and bladder neck and a careful plication of

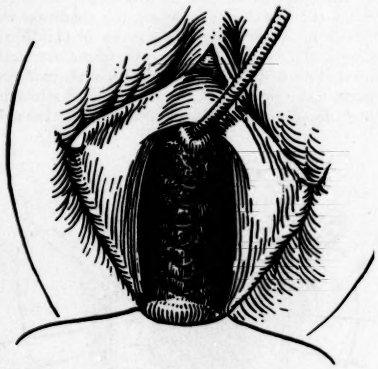

FIGURE 6.
The mucous membrane is closed, thus completing the operation.

the pelvic fascia and urogenital diaphragm over these structures. This serves to support the urethra and bladder neck from below and to hold them up behind the pubic arch. The steps of this operation are illustrated in Figures 1 to 6. It is essentially the method advocated by Young[18] in 1922. There were cures in 15 cases, or 71 per cent.

Various types of suture material were used in the repair, including catgut, cotton and silk. Little difference in the results was noted, although catgut seemed to be the best material, perhaps by virtue of a greater inflammatory reaction, with more scar-tissue formation.

A repair of the perineum was carried out in all cases to improve the pelvic support by approximation of the levator ani muscles.

One patient in each of the above groups was changed from being only improved to being cured by the use of periurethral injections of 5 per cent sodium morrhuate. The same treatment on a number of other patients who were not cured gave no improvement.

Complications

One patient developed a perivesical hematoma that became infected and required drainage. In another case a cystocele occurred following the operation, and a later repair of this was necessary.

Three patients developed urethrovaginal fistulas requiring repair. It is believed that this may have been due to anchoring the mucosa to the underlying layer in the completion of the closure (Fig. 5), and this procedure has been abandoned.

SUMMARY

The anatomy of the internal (involuntary) and the external (voluntary) sphincter mechanisms of the bladder and urethra in women are briefly described.

The relative importance of damage to the voluntary and involuntary sphincters in the production of stress incontinence is discussed.

Various operative procedures used for the cure of stress incontinence are briefly described.

Sixty-three operations were performed in 62 patients for exertional urinary incontinence resulting from childbirth trauma. The operation was successful in 44 cases, or 70 per cent.

Stress incontinence is believed to result when the function of the involuntary sphincter mechanism is impaired owing to stretching and distortion of the bladder neck and proximal urethra. This occurs after trauma that allows these structures to sag away from their normal positions behind the pubic arch. The voluntary sphincter may be damaged in the process, but such damage is of little, if any, importance in the production of stress incontinence.

The success of an operation for stress incontinence is considered to depend on the restoration of the bladder neck and urethra to their normal anatomic positions, allowing the involuntary sphincter to resume its normal function.

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Discussion

Dr. Edward L. Young (Boston): I should like to emphasize what I believe to be the cause of at least 30 per cent of the failures in this type of operation. These cases must be studied intensively beforehand, because there are many conditions that may make trouble. One is called a "reno-vesicle reflex" — a complicated name for something that is not understood, but it means that because of minor damage to the kidneys there are often bladder symptoms, including incontinence. Infection, which occurs in spite of a perfectly clear urine that is chemically normal, can also cause incontinence.

I believe that some failures are due to the fact that these conditions are not recognized. Last year I had an interesting case of failure. I closed what I was sure was a stress incontinence, and the patient was worse when I got through than before I started. I discovered that urine was draining from the cervix. Further study showed that the patient had had a supravaginal hysterectomy. The surgeon had carefully put a stitch through the cervix and the bladder, where there was a valve. When the valve opened the urine poured out through the cervix.

I believe that about every quarter of a century this subject must be studied because it is a bothersome problem to a great many women, and the best method is careful dissection, such as that described by Dr. Bartlett, to identify the layer that is a mixture of fascia and muscle tissue. If the cases are selected, I think that the cures will approximate 85 per cent.

Dr. Stephen Rushmore (Boston): I have been interested in this subject for many years, and after operations for this condition I have found so many failures that I hope I have learned something from my experience.

In the first place, a satisfactory test of where the difficulty lies can be made by the use of a Pezzer catheter — not an old one from which the life of the rubber has been boiled out, but a new one that has some rigidity. If such a catheter is introduced and drawn down against the internal meatus of the urethra, the opening of the bladder, it can usually be determined easily that that is the point at which the weakness exists and at which resistance must be built up.

It seems to me that the cause of the failures in many of these cases is the fact that the sphincter muscle — the smooth muscle that is the wall of the bladder and is hypertrophied at this point — is stretched throughout its whole circumference, owing to injury at childbirth. If it is stretched more on the anterior or upper margin, there will be greater difficulty in repair of the organ or the structure so that it will function properly.

If the muscle is stretched at that point, the logical approach seems to be to repair it from above, an impractical method of attack. But that explains, I believe, why sewing it up from below in some cases gives such a poor result, because the muscle itself has been weakened at the anterior and upper margin.

I think that the results may be improved by careful plastic operation and placing of sutures — it is the placing of the suture that is of greatest importance — and the testing of the amount of contraction resulting from the operation by the use of the Pezzer catheter.

In some of these cases in elderly women there is the trauma of many childbirths, and the tissue seems to have lost its tone; the muscle itself has lost most of its tone and is extremely flabby. A perfectly satisfactory functional result with a muscle that is practically exhausted cannot be expected in every case.

INFECTION CAUSED BY *STREPTOBACILLUS MONILIFORMIS**

Report of 2 Cases Following Rat Bites

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BOSTON

INFECTION due to *Streptobacillus moniliformis* is often characterized by fever, a migrating polyarthritis, a skin rash and a relapsing course. A preceding history of rat bite within ten days is frequent. In a few reported cases, however, no source of infection could be established.[1, 2] Place, Sutton and Willner[3] described an outbreak occurring in Haverhill, Massachusetts, following the ingestion of raw milk. Organisms isolated from 11 of 13 patients in this epidemic were extensively studied by Parker and Hudson,[4] who described them as a new species, *Haverhillia multiformis*. Unknown to them at the time, however, Levaditi and his associates[1] had isolated and described the organism a year previously as *Str. moniliformis*. The most complete review is that of Brown and Nunemaker.[5] Watkins[6] recently summarized 39 cases of rat-bite fever reported in the United States in which *Str. moniliformis* was the proved etiologic agent. Positive blood cultures were obtained in the 2 cases described below.

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Case 1. C. J., a 5-month-old infant, was admitted to the hospital on January 29, 1940, after having been severely gnawed by a rat. Physical examination showed a pale infant with a temperature of 102°F., regular respirations and a rapid pulse. There were bites on the right cheek and a large defect in the right wrist, in addition to tooth marks over the right hand.

The right wrist was débrided and irrigated. During treatment pieces of cartilage floated up through the defect. A culture of the wound grew out *Str. moniliformis*, as did a blood culture taken on admission. Examination of the blood revealed a red-cell count of 2,220,000, with a hemoglobin of 43 per cent, and a white-cell count of 18,000, with 43 per cent neutrophils, 52 per cent lymphocytes, 4 per cent monocytes and 1 per cent basophils.

The temperature fell to 100°F. in 3 days. After a week the temperature alternated between normal and 100°F. until discharge. Chlorinate dressings and irrigations were applied to the wound daily, with steady healing and improvement, in spite of an x-ray diagnosis of osteomyelitis in the underlying bones. A blood Hinton test was negative on March 1. On April 28 the patient was sent to a convalescent home.

It is of interest in this case that in spite of extensive rat bites, from which *Str. moniliformis* was cultured directly, and an early bacteremia, the disease did not progress to a full picture of rat-bite fever. No skin rash or polyarthritis was noted.

Case 2. P. S., a 75-year-old Jewish man, was admitted to the hospital on June 14, 1946, because of fever. A rat had bitten him on the forehead 3 days previously. On the day of admission the patient had fever, chilly sensations, headache, backache and pains in the knees.

Physical examination revealed a well developed and well nourished man lying comfortably in bed. Physical examination was essentially negative except for injection of the conjunctivas and a dry, coated tongue. No skin rash was present. The small wound on the forehead had healed. There was no tenderness, swelling, redness or pain on motion of the joints.

The temperature was 100°F., the pulse 84, the respirations 40, and the blood pressure 120/76. Examination of the blood revealed a hemoglobin of 100 per cent (Sahli) and a white-cell count of 12,300, with 93 per cent neutrophils and 7 per cent lymphocytes. Urinalysis was negative.

The patient was given 40,000 units of penicillin every 3 hours. Within 24 hours he became asymptomatic. The temperature fell to normal within 3 days. Penicillin treatment was continued until June 23, the day of discharge.

On June 20 the white-cell count had fallen to 7900. Blood Hinton tests were negative on July 3 and on July 27.

The blood taken on admission was cultured in a meat-infusion broth.* Within 24 hours there was a fairly abundant growth of *Str. moniliformis*, as determined by the characteristic "fluff ball" appearance of the colonies and the presence of pleomorphic, gram-negative organisms on smear. Identification was further confirmed by agglutination tests. Antiserums previously prepared in rabbits against three strains of *Str. moniliformis* — two from patients with rat-bite fever and one from a rat — were used for this purpose. Agglutinations using the patient's organism as antigen were obtained in all three serums in a titer of 1:6400. Agglutinin absorption tests were set up to determine whether the freshly isolated strain was identical with the other three. Two of them proved to be identical with the patient's organism. The third strain was a distinctly different type.

Agglutination tests, in which the patient's organism was run against his own serum, showed a marked rise in titer of immune bodies. None were found on June 15, but the titer had risen to 1:160 on July 3 and to 1:320 on July 27. Parallel agglutination tests on the first two dates were negative with dysentery polyvalent, *Pasteurella tularensis* and *Brucella abortus* antiserums.

On first isolation the organism showed a pronounced virulence for mice: 0.5 cc. of a 24-hour culture in 10 per cent ascitic broth, when injected into each of 5 mice intraperitoneally, led to death in 24 hours. After repeated transfers the mouse virulence was lost. The Streptobacillus was markedly pleomorphic in the peritoneal cavity, but appeared as short, gram-negative rods when isolated by smear from the heart's blood.†

A penicillin sensitivity test revealed that the organism was killed by an in vitro concentration of 0.0156 units per cubic centimeter.‡

Subsequent blood cultures on June 19 and July 3 showed no growth.

This patient did not show any of the characteristic clinical signs of rat-bite fever. Since massive doses of penicillin were begun within twenty-four hours of the onset of the illness, however, and since the Streptobacillus isolated was extremely sensitive to the drug, the absence of such findings is not surprising. The illness began after a characteristic incubation period following the rat bite. Isolation in pure culture and the demonstration of a significant rise in titer of agglutinins during convalescence demonstrated that the infection was caused by *Str. moniliformis*. The course of the disease did not favor an attempt to isolate *Spirillum minus*.

The outstanding feature of infections due to *Str. moniliformis* is the predilection of this organism for synovial membranes, which results in a migrating polyarthritis. Arthritis is characteristic of spontaneous outbreaks of the disease in mice.[7, 8] Buddingh[9] has recently shown that the Streptobacillus, when inoculated onto the chorioallantoic membrane of the chick embryo, leads to pathologic lesions that are localized primarily in the joints. Joint involvement is not invariably present in this type of rat-bite fever, although it occurs in a high percentage of cases.

In the cases presented above the characteristic manifestations of rat-bite fever did not appear. The early institution of penicillin treatment may explain the short course in Case 2. In Case 1 it is possible that the organism was of low virulence. One may also speculate that in some cases the infection is limited to a mild bacteremia. This might be found if patients coming to a surgical outpatient department for rat-bite treatment were subsequently followed with blood cultures.

The efficacy of penicillin treatment in cases of rat-bite fever has been described by a number of authors. Altemeier and his co-workers[10] and Wheeler[11] noted rapid clinical improvement with penicillin. The sensitivity of the organism in Case 2 puts it in the range of bacteria most susceptible to the drug, such as pneumococci and streptococci.

Contrary to the experience of Brown and Nunemaker,[5] the culture of *Str. moniliformis* has not been found difficult. Meat-infusion broth is sufficient for blood culture on primary isolation. The best growth, however, is obtained in infusion broth with the addition of 10 to 15 per cent ascitic fluid. Within twenty-four hours the growth appears as large aggregates of colonies near the bottom, suspended in a clear liquid. The organism can be maintained on blood-agar plates incubated in a candle jar. Transfers at weekly intervals have been sufficient to maintain three different strains for several years.

In Case 2 the agglutination titers rose to 1:160 and 1:320, although the patient had apparently harbored the Streptobacillus for only a short time. Brown and Nunemaker[5] concluded from a serologic study of the serums from 120 control cases that a titer of 1:80 or above was definitely diagnostic of infection with *Str. moniliformis*. The natural growth of the Streptobacillus as aggregates of colonies in broth is unsuitable for the performance of agglutination tests. Suitable suspensions of antigen were obtained when a twenty-four-hour broth culture was agitated in a shaker for thirty minutes at moderate speed.

"Rat-bite fever" is a term used to cover two separate infections — one caused by *Str. moniliformis*

*Acknowledgment is made to Miss Marion E. Lamb, bacteriologist, Boston City Hospital, for her helpful suggestions regarding the bacteriology in this case.

†This phenomenon has been described by Parker and Hudson.[4]

‡Test performed through the courtesy of Miss Clare Wilcox, Thorndike Memorial Laboratory, Boston City Hospital.

and the other by *S. minus*. The diseases caused by these organisms may be clinically indistinguishable, owing to overlapping symptomatology. Both respond well to penicillin therapy. Dawson and Hobby,[12] supported in a discussion by Blake, have questioned whether the laboratory evidence has been sufficient in all reported cases to support a diagnosis of infection with *S. minus*, since mice used for blood inoculations may naturally harbor the Spirillum. It has been established by inoculations of paretic patients with *S. minus*, however, that this organism can cause a disease in man with both skin rash and polyarthritis.[13, 14] One wonders, nevertheless, whether the Streptobacillus might not be found more often if properly looked for in cases of rat-bite fever. No case reports have been found in the literature in which both organisms were found. Brown and Nunemaker[5] present evidence that *Str. moniliformis* is the most frequent infecting agent following rat bite.

Summary

Two cases of infection with *Streptobacillus moniliformis* are reported. The simplicity of culturing this organism and of agglutination tests is stressed. Penicillin was extremely effective in 1 case.

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SURGICAL TREATMENT OF DEGENERATIVE ARTHRITIS OF THE KNEE JOINT*

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SINCE the conservative treatment of degenerative or hypertrophic arthritis of the knee joint had been disappointing at the Lahey Clinic, particularly in vigorous patients with unilateral involvement, a plan of surgical management was decided on, and in 1940 the results obtained in knee joints that had been operated on in 20 cases were reported.[1] Since then sufficient time has elapsed to evaluate the results in an additional 10 cases. The object of this paper is to discuss criteria for selection of patients for surgery, to present details of the operative technic and finally to report the results obtained.

Selection of Patients

The importance of careful selection of patients for knee-joint surgery, especially when joint function is maintained, cannot be too strongly emphasized. In each case a detailed medical examination is carried out, and if the physical status indicates that major surgery on the knee is feasible, in addition to the orthopedic survey, the patient is considered from the standpoint of his ability to co-operate and to follow out tiresome and often painful exercises, and in particular, an estimate is made of his desire or drive to return to comparatively normal activities. Provided that the patient's physical condition permits major surgery on the knee and the other requirements are fulfilled, operation is advised. It is understood that of many patients who have degenerative arthritis of the knee joint, relatively few meet the standards for surgery as herein described. But if the cases are carefully selected on the basis of the points outlined, the results have been superior to those obtained with other methods.

In patients with unilateral joint involvement in whom the preoperative studies indicate an advanced destruction of the joint, the significance of these data is emphasized; the patient is advised to permit an arthrodesis if on joint visualization the preoperative impressions are confirmed.

Operative Technic

The knee joint was first explored through a medium parapatellar incision. Later, in patients with marked hyperplasia of the patella, a midline incision was employed, the patella removed by sharp dissection, and the remainder of the operation performed under excellent visualization. In cases

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with advanced degenerative changes that indicated possible arthrodesis, the inverted "V" incision in the capsule, as described by Coonse and Adams,[2] has been most satisfactory.

In the planning of a surgical procedure for the treatment of degenerative arthritis of the knee joint, repeated clinical observations indicated that the following structures in particular were to be considered: the hyperplastic synovial membrane; the patella; the articular cartilage covering the femur and tibia and marginal exostoses; and the meniscuses.

If definitely scarred and hyperplastic, the synovial membrane was removed from the anterior portion of the joint, together with the fat pad. In none of these patients was the posterior compartment explored. Likewise, when the meniscuses were degenerated, they were carefully excised back to the posterior attachment.

The patella was either markedly reduced in size or removed entirely. The clinical impression that the region of the patella was a source of injury was borne out by the gross and microscopical studies of Keefer et al.[3] in pathologic studies of a hundred knee joints from 77 consecutive cases at autopsy. Death resulted from a variety of causes, and the cases were not selected on the basis of previous clinical findings, diagnosis or presence of symptoms in the joint. These authors found that anatomic changes were often observed at the points that, in turn, had been subjected to the greatest movement, weight and pressure. In particular, degenerative changes were described at the median horizontal facet of the patella and along the patellar groove of the femur. In other words, the two regions of the knee that generally exhibit degenerative arthritis are in relation to the patella.

After a careful review of the literature, notably the results obtained by Brooke,[4] who excised the patella for comminuted fracture, it was decided and proved that the patella could be either reduced in size or entirely removed without impairment of knee-joint motion.

The remaining steps of the operation comprise removal of marginal exostoses and shaving down of the fibrillated cartilage over the articular surfaces of the femur and tibia. This cartilage is often markedly degenerated, and it should be shaved down to a firm base; the operator should ensure that there are no rough spots to cause irritation. In this connection Magnuson,[5] in 1941, reported good results in a large series of cases in which synovectomy was not performed and in which the patella was never entirely removed. This author emphasized that "the success of the procedure depends on the complete removal of all mechanical irritants from the joints." I am in complete accord with this statement and for that reason believe that in patients with long-standing, pronounced chronic hyperplasia the synovial membranes should be taken out and the patella either cut down or removed.

The joint capsule is closed with interrupted silk, the subcutaneous tissue with interrupted fine chromic, and the skin with wire sutures. Use of the last material permits the sutures to remain in place ten to fourteen days postoperatively, while active muscle exercises and motion in the joint are instituted. The resultant scars have been much less obvious than when the skin was closed with other types of sutures. Large, fluffy sections of gauze pads are placed about the knee, and a firm pressure bandage applied to the entire extremity. Initially, patients are more comfortable in a plaster cast, but return of joint motion is delayed in comparison with cases in which only a pressure bandage is utilized.

When an arthrodesis of the knee was performed because of advanced destruction of the articulation, a long leg plaster cast over a pressure dressing as described comprised the immediate postoperative fixation. Two weeks after operation the cast was removed, and a Stader unit[6] applied, fixing the position of the femur to the tibia and thereby maintaining excellent contact of the bony surfaces. This remained in place six to eight weeks. When the unit was then removed, clinical union between the two bones was often apparent. Thereafter, the patient was ambulatory and walked in a long leg plaster cast, bearing gradually increasing weight until roentgenograms indicated that sufficient union had occurred to permit application of a long leg caliper. The brace was removed when fusion was firm.

After the report by McKeever[7] on the use of cellophane, the possibility of employing this medium was considered for these operations. But because of the satisfactory results obtained on the program of therapy as outlined and particularly because of my uncertainty regarding the eventual state of the cellophane, I decided not to add this element.

Postoperative Care

In the average case motion was begun on the fourth or the fifth day. Patients with adequate muscle control, particularly if they had received adequate preoperative training in muscle exercise, began motion on the third day. In others, motion was begun later. In all patients the extremity was intermittently suspended just above the ankle region by a sling attached to an elastic cord from an overhead frame. This permitted relatively early active exercise with a minimum degree of discomfort. Local heat and light massage were routinely carried out. Weight bearing was started within two weeks, under careful guidance. In an average of 3 out of 4 patients, gentle manipulation of the knee joint was performed under intravenous Pentothal anesthesia within three weeks after operation. It was found that this step materially expedited

return of normal joint flexion. With one exception there were no untoward reactions following this maneuver.

Results

With the objective of maintaining knee motion, 30 patients were operated on, and in 5 additional patients an arthrodesis was performed. In each case only one knee was treated. The average age of this group was fifty-seven years. There were failures in 3 cases. One has already been reported as being due to the presence of a mixed arthritis[1]; 2 patients did not co-operate in carrying out the postoperative exercise regimen. Of the 5 patients submitted to arthrodesis, a firm bone fusion was obtained in each knee joint. The follow-up period ranged from seventeen months to seven years, with an average of twenty-six months.

Of the remaining 27 patients operated on to improve joint function, all exhibited postoperative increase of knee motion. Normal active extension of the lower leg on the thigh was observed in all cases. The minimum range of flexion was 65°, whereas the maximum was normal. In this group, 21 patients had a normal range of motion. In every case the articulation was stable, and swelling of the knee was not observed. Twelve patients denied any symptoms referable to the joint; 8 reported intimate aching pain in the knee after exposure to severe cold and damp weather. Seven patients described intervals of apparently mild discomfort after a rest period preceded by marked physical activity.

In summary, all this group emphasized that they did not suffer severe pain and that their symptoms were in no sense comparable to those experienced before operation.

With the exception of a case previously reported, the follow-up roentgenogram showed essentially no change as compared with the immediate postoperative film, and in no case did the subsequent film reveal the pronounced degenerative arthritis evidenced in the preoperative roentgenogram.

* * *

In patients with pronounced disability due to degenerative arthritis of the knee joint, who had been selected on the basis of their physical fitness for operation and in particular for their willingness to co-operate with the postoperative regimen described above, and with the objective of maintaining knee motion, the surgical procedure detailed in the text resulted in marked amelioration of symptoms. In a smaller group of patients who were incapacitated because of marked destruction of the joint as shown at operation, arthrodesis resulted in complete relief of pain while allowing greatly increased physical activity. Over a follow-up interval ranging from seventeen months to seven years, observations on this group of 35 patients confirm the belief that the surgical treatment of degenerative arthritis deserves an important place in the physician's armamentarium.

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FAVISM*

A Short Review and Report of a Case

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FAVISM is an acute hemolytic anemia following contact with beans or pollen of *Vicia faba.* It has been classified among the paroxysmal hemoglobinurias,[1] and manifests itself by the so-called "hemolytic syndrome," which, in view of its specific action on the red cells, might better be named the "erythroclastic syndrome." The main characteristics are a fulminant onset, jaundice, anemia and hemoglobinuria. Favism is probably an allergic phenomenon that is due to a hypersensitivity to the ingestion of the beans or to inhalation of the pollen of *V. faba,* a large yellowish bean of the lima-bean family.

The condition is exceedingly rare in the United States, although not infrequent in Sicily, Sardinia and southern Italy. Apparently, only 2 cases have been reported in English, and these occurred in Italian-born adults who had immigrated to the United States.[2] The case reported below therefore appears to be the first case in an American-born child, although the patient was of Italian extraction.

Favism is a comparatively old disease. It was known to Herodot, Pythagoras and Empedocles, and the condition is stated to have been quite widespread and grave, at times, in ancient Egypt and other Mediterranean countries.[3] The first modern authors to report it were Messina in 1851, La Grega in 1856 and Di Pietra in 1858. The first to forward the idea that favism was due to an idiosyncrasy was Bertòlo in 1873.

An excellent paper about favism was written by Gasbarrini,[3] who found a hereditary factor in about 20 per cent of cases. He observed that neuropathic, anemic and "lymphatic" persons were somewhat predisposed to the affliction. Gasbarrini refuted the theory of the older Italian authors that favism was caused by an infectious agent — possibly a fungous infection of the bean — and attributed the disease to a "toxin." A similar opinion was held by Fermi and Martinetti,[4, 5] who reviewed 1211 cases.

Preti,[6] who, as director of the University Clinic of Sassari in Sardinia, had ample occasion to observe a number of cases, maintained that the theory of a toxin was untenable because of the bizarre way in which the disease struck. He believed that favism was caused by an anaphylactic reaction.

The first of the cases in the English language mentioned above was reported by McCrae and Ullery,[7] who described a rather severe attack of hemoglobinuria and the usual symptomatology following the ingestion of fava beans in a fifty-three-year-old Italian-born man. In his youth the patient had had several episodes of unconsciousness while walking through fields of blossoming fava plants in Sicily; all these episodes had been followed by hemoglobinuria. After a diagnostic skin test this patient had a recurrence of some of the symptoms. The second case, reported by Hutton,[8] occurred in a twenty-year-old Italian-born man who, besides the usual symptomatology, had a definite family history of occurrence in his grandfather, grandmother, mother and a brother. This patient gave a negative skin test.

The majority of cases have been reported from Sicily, Sardinia and the southern provinces of Italy. There are also a few reports from Germany.

Favism has quite a definite seasonal incidence, most cases being observed between April, the season of blossoming of the plant, and June to July, when the fresh, mature bean appears on the market. Gasbarrini[3] noted that prolonged rain hindered the development of favism in a given year.

Heredity seems to play a definite role in about 20 per cent of cases. There are reports of entire families who are hypersensitive to the fava bean, as in Hutton's[8] report. In the remaining 80 per cent no hereditary factor is evident. There is apparently no predilection for either sex, both being affected about equally. The majority of cases occur during childhood and adolescence, but the disease is by no means limited to the first two decades of life and cases have been reported in elderly people.

In the series of 1211 cases reported by Fermi and Martinetti,[4] 459 were caused by inhalation of the pollen from the blossom of the plant, 725 were due to ingestion of the bean, and 27 had an undetermined etiology. Autopsies have been recorded in only 2 cases, in both of which the exact mechanism of the pathogenesis was rather inconclusive.[2] Both examinations showed a generalized hyperemia and an increase in the size of the liver, the kidneys and the spleen. The spleen was reported as being three times its normal size in 1 case. According to Hoffman and Kracke[1] a hypersensitivity to one of the protein substances present in the pollen as well as in the bean is created through repeated contact — either by inhalation or by ingestion — and is followed by destruction of erythrocytes, leading to the hemolytic-hemoglobinuric syndrome. The authors maintain that the syndrome does not occur on the first contact with the bean or its

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pollen, but only after subsequent exposure. In animal experiments no anaphylactic reactions were observed unless the animals had previously been sensitized to the fava bean by means of feeding or by injection of extracts.

The exact mechanism of how the hemolysis is produced is not too well understood. Preti[6] reports that even sucklings were afflicted when the mother or the wet nurse ate fava beans, and in his cases the mother did not necessarily present the symptoms herself. He also noted that the condition was rare in persons who ate fava beans regularly throughout the year, and he assumed that this was due to a desensitization.

The incubation time between inhalation or ingestion and the onset of the first symptoms may be one to three days or only a few minutes. Thus, McCrae and Ullery's[7] patient stated that he became unconscious while walking through the blossoming fields.

The usual prodromal symptoms include fatigue, weakness, headache, pain in the upper or lower extremities, anorexia, nausea, vomiting, abdominal pain, diarrhea and, in severe cases, unconsciousness. From one hour to one or two days after these manifestations hemoglobinuria begins, with marked prostration and at times with shock. At the same time the skin shows an ashen-gray pallor simultaneous with a moderate jaundice.

Depending on the degree of severity there are, according to Gasbarrini, five different forms: the abortive form, which is characterized by headache, nausea, pain in the upper and lower extremities, pallor of the skin and mucous membranes and absence of hemoglobinuria; the mild form, which is characterized by these symptoms, in addition to moderate anemia, slight icterus, slight hemoglobinuria and, usually, spontaneous recovery within a week; in the grave form, which may be deadly and which strikes soon after the ingestion of fava beans, the patient presents extreme weakness and prostration, marked pallor and moderate icterus of the skin and scant and markedly bloody urine — children often suffer from diarrhea and vomiting of bile; the fulminant form, which principally affects children and presents a sudden and intense anemia and hemoglobinuria and in which death from shock frequently occurs within the first twenty-four to forty-eight hours; and the so-called "hemorrhagic form," which is characterized by petechiae and ecchymoses and is extremely rare and nearly always fatal.

On physical examination an enlarged spleen may or may not be found. The liver is often slightly enlarged and moderately tender. The other abdominal organs usually do not show any pathologic change. Except in the rare hemorrhagic form there are no cutaneous manifestations of hemorrhage. The scleras are moderately jaundiced, and the skin shows the combination of pallor and icterus described above. The patient is usually apathetic and listless, and may be in profound shock.

The blood picture is that of a severe normocytic anemia, and the hemoglobin may be as low as 20 per cent and the red-cell count as low as 1,000,000. Some anisocytosis, poikilocytosis and polychromatophilia are present, but neither spherocytes nor target or oval cells have been reported. The fragility of erythrocytes to hypotonic sodium chloride solutions is usually within normal limits. Tests for acid, mechanical and heat fragility[9, 10] have apparently never been made in this condition.

In the initial stage the blood reveals a leukopenia, a neutropenia and a thrombocytopenia. Shortly thereafter leukocytosis begins, and the blood may even present a leukemoid picture. The platelets also begin to increase in number and may go as high as 900,000, which according to Preti[6] gives the case a favorable prognosis.

The blood chemical findings usually indicate a markedly increased icteric index, a moderate to marked bilirubinemia and a negative direct and a positive indirect van den Bergh reaction.

The urine may vary from a slight pinkish discoloration in abortive cases to a deep brick red in the severer forms. It may contain a few red cells and usually reveals a ++++ test for albumin and a number of casts. The guaiac test is often ++++. The urine and stool show a moderate to marked increase of urobilinogen; the stool is brown, and the urine may contain some bile pigment.

In spite of its stormy and alarming onset, favism is a comparatively benign disease. The majority of patients recover. The mortality rate is 8 per cent, death occurring either in the initial stage of shock or later from anemia. The clinical course is apparently not influenced by the amount of ingested beans, minimal amounts having led to quite protracted illness and large portions having been followed by rather speedy recoveries. McCrae and Ullery's[7] patient required hospitalization for thirty-eight days, whereas Hutton's patient was out of bed on the fifteenth hospital day.

No treatment may be required in the abortive cases, but in the severer forms, the most effective therapy is the immediate institution of compatible blood transfusions. These transfusions should be repeated daily as long as hemoglobinuria and other evidence of erythroclastic activity are present. For the initial stage of shock adrenalin has been recommended. The obvious prophylaxis is for the hypersensitive subject to avoid ingestion of the bean or inhalation of its pollen.

In the following case transfusions of whole citrated blood resulted in recovery.

A 3½-year-old, American-born boy of Italian extraction was admitted to the hospital on July 29, 1946, with the chief complaint of "bloody urine" of 16 hours' duration. The history, as obtained from the somewhat panicky parents, revealed that on the evening prior to admission the child had expressed a desire to urinate but had stated that he

had pain in both knees and was too weak to walk to the bathroom. The mother had carried the child to the bathroom and had noticed that the urine was bloody. The family physician stated that the urine showed a ++++ test for albumin but that he was unable to find any blood cells on microscopical examination. The bloody color of the urine increased in intensity during the night and the following morning, and the mother noticed that the skin had become somewhat jaundiced. The patient's general condition grew worse, he became more and more prostrated, and at noon, when he was admitted to the hospital, he appeared in extremis.

Both parents were exhaustively questioned about the past history in an effort to obtain a lead regarding the nature of the condition. They denied any instance of a similar episode in any of the close or remote members of the family at any time. There was no history of exposure to malaria, of syphilis or antisyphilitic treatment, of exposure to cold, of swimming at the beach, of any physical exertion, of sulfonamide or acetanilid medication or of contact with lead, other blood-destroying chemicals or carbon monoxide. There was no history of a spider or a snake bite or of ingestion of mushrooms or of fava beans. The child had been in good health since birth, no anemia having appeared before the present episode.

Physical examination revealed a well developed and well nourished boy who appeared to be moribund. He was extremely weak, apathetic, listless and, at the same time, irritable. The skin was both markedly anemic and markedly icteric, showing a combination of an ashen-gray pallor and a deep jaundice. The head was essentially normal except for moderately jaundiced scleras. The conjunctivas and other mucous membranes were extremely pale. The ears, nose and throat were essentially normal. There was no cervical or other adenopathy. The trachea was in the midline; the thyroid gland was not palpable. The chest was clear and resonant to percussion and auscultation, and there were no audible rales. The cardiovascular system presented a marked tachycardia (160 per minute), a regular sinus rhythm, no enlargement of the heart, no murmurs and no thrills. The heart sounds were of good quality. The abdomen was soft and nontender, and no masses were felt. The liver was slightly enlarged, the edge extending 1 cm. below the costal margin; the spleen was not palpable. The extremities were essentially normal. The skin presented no pathologic changes except the discoloration described above. There were no petechiae, ecchymoses, evidence of insect or snake bites or interruption of the continuity of the skin at any place. The reflexes were physiologic.

The temperature was 102°F., the pulse 160, and the respirations 30.

Examination of the blood showed a red-cell count of 1,140,000, with a hemoglobin of 4.2 gm. (29 per cent), and a white-cell count of 20,500, with 72 per cent neutrophils, 24 per cent small lymphocytes, 2 per cent monocytes, 1 per cent eosinophils, 1 per cent basophils and 1 per cent normoblasts. There was slight anisocytosis and moderate polychromatophilia. The platelet count was 248,000. The bleeding time was 90 seconds, and the clotting time 150 seconds. No spherocytes or target, oval or sickle cells were seen. There was no latent sickling. The mean corpuscular volume was 91 cu. microns. The reticulocyte count was 4.2 per cent. The blood group was AB, and the patient was Rh+. A fragility test showed initial hemolysis at 0.44 in the patient and at 0.40 in the control and complete hemolysis at 0.28 in the patient and at 0.32 in the control. The icteric index was 57 units. The van den Bergh test showed a negative direct and a positive indirect reaction. A stool was negative for blood but positive for bile. The urine revealed an increased urobilinogen and some bile. It was positive for albumin and negative for sugar, and the sediment showed many coarse granular casts. The guaiac reaction was ++++, but no red cells were found in the urine.

It was evident that there was, not hematuria, but hemoglobinuria, which is, of course, nothing but the urinary manifestation of marked red-cell destruction, and consequently a hemolytic or erythroclastic syndrome whose origin was obscure. A hemolytic crisis of a familial congenital hemolytic anemia was ruled out by the absence of spherocytes, of an enlarged spleen, of a pre-existing mild anemia and of a positive family history.[11, 12]

The blood picture was neither that of a Cooley's anemia (thalassemia or Mediterranean syndrome) nor that of a sickle-cell anemia,[13] the latter being considered as a possibility because it occurs occasionally in patients of Italian extraction.[14] The condition was too acute and too alarming for a Marchiafava–Michele syndrome, and from the history, black-water fever, cold hemoglobinuria, march hemoglobinuria, favism or toxic hemolysis of any known mechanism could be excluded. The only condition that seemed to fit this case appeared to be Lederer's anemia,[15] a condition that has often been misused as a catchall for hemolytic syndromes that cannot otherwise be classified.

Fortunately, on the 3rd hospital day, the mother, who had recovered from her initial panic, remembered that on the day of the onset of the disease the child had had a large meal of fava beans. She admitted that she had "forgotten all about it" owing to the excitement about the child's alarming condition. Consequently, the diagnosis was changed from acute hemolytic anemia of the Lederer type to favism. This revelation did not affect the therapy or the clinical course in any way, since the treatment for both conditions is identical.

Immediately after admission a transfusion of 300 cc. of whole citrated blood was given. Toward the end of the transfusion the temperature rose to 106.8°F., following a chill of 10 minutes' duration and a convulsion lasting about 2 minutes. The pulse was 160, and the respirations went up to 60 and were labored. A moderate cyanosis was observed. The rise in temperature was probably a transfusion reaction, but because the diagnosis was uncertain it was considered advisable to administer 50,000 units of penicillin initially and 25,000 units every 3 hours.

On the following day the whole picture had changed rather dramatically. There was still the same amount of hemoglobinuria, with increased urobilinogen, and a ++++ guaiac reaction, but the temperature had fallen to 100.4°F., the pulse to 120, and the respirations to 40. The color of the skin was definitely improved, with less anemia and no cyanosis. The hemoglobin had risen to 7.6 gm. (52 per cent), and the red-cell count to 2,400,000. The patient was less apathetic and began to answer when spoken to.

For 5 consecutive days 250 cc. of whole citrated blood was administered daily with a consistent change in the blood picture (Table 1). The clinical condition continued to improve

TABLE 1. *Significant Laboratory Data.*

HOSPITAL DAY	RED-CELL COUNT	HEMOGLOBIN	
	×10⁶	gm.	%
1	1.1	4.2	29
2	2.4	7.6	52
3	3.0	8.5	58
4	3.8	10.7	74
5	4.1	12.2	84
8	4.7	13.1	90

rapidly, and the temperature fell to and remained at normal levels; the hemoglobinuria disappeared, the urobilinogen value becoming normal on the 4th day. The jaundice and anemia cleared up gradually, and on the 8th hospital day the patient was discharged.

An interesting feature in this case was presented by the spleen, which on the day of admission was not palpable. On the second hospital day a slight enlargement appeared, and on the third day the spleen was definitely firm and enlarged, the edge extending two fingerbreadths below the costal margin and being rounded. The size of the spleen remained unchanged until the sixth hospital day, when it became softer and decreased until it was no longer palpable on the eighth day.

The diagnosis of favism is said to be easy when it occurs in one of the usually stricken regions of southern Italy and when a history of ingestion of

fava beans or inhalation of the pollen is obtainable. In the case presented above, that of an American child with an emphatic denial of contact with *V. faba*, the diagnosis was not made at first. After all known erythroclastic (hemolytic) syndromes had been ruled out, an erroneous admission diagnosis of acute hemolytic anemia of the Lederer type was made; the diagnosis was changed only on the third hospital day, when a history of ingestion of fava beans was elicited.

Such an error is understandable, since the onset, clinical picture and clinical course of Lederer's anemia[16] are similar to those in the case presented above; for that reason the disease has been called *anémie en coup d'archet* by French authors.[17] It is quite possible that some of the less well understood of the 60 cases of Lederer's anemia reported in the literature[18, 19] — whose etiology is unknown and was attributed by Lederer himself to an infectious process — can be explained by an allergic phenomenon similar to or even identical with that in the case presented above. Since fava beans are regularly eaten by a large number of people without producing symptoms, even in the person who may suddenly develop a marked erythroclastic process, it seems not improbable that a previous fava bean meal has been forgotten by the patient and escaped the attention of the physician.

Summary

A case of favism that is apparently the first reported in an American-born child is presented. In two previous reports in the literature in English, both cases occurred in immigrants who had been born in southern Italy.

The diagnosis of favism was not made initially because the anxiety-stricken parents denied that the patient had eaten fava beans. This was admitted only on the third hospital day, after which the diagnosis was apparent.

The question is raised whether some of the obscure cases of acute hemolytic anemia of undetermined origin in the literature had a similar etiology.

In the case presented the onset of the condition was alarming, but the patient's response to daily blood transfusions was such that in eight days he was discharged from the hospital, entirely recovered.

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MEDICAL PROGRESS

RUBELLA (GERMAN MEASLES) (Concluded)*

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Flibbertigibbet

In folklore congenital deformities were considered to be the result of extrinsic influences on the pregnant mother. Something she saw or some experience she underwent was thought to bring about the defect in her child. At the time when there was a general belief in witchcraft and calamities were ascribed to demoniacal influence, congenital deformities were supposed to be the result of the casting of a spell on the pregnant mother. *King Lear* contains the following reference: "That foul fiend, Flibbertigibbet. He begins at curfew, and walks till the first cock. He gives the web and the pin, squints the eye, and makes the harelip." The "web and the pin" is an old term for cataract. Flibbertigibbet was merely an unseen character referred to in a play, but people firmly believed in witchcraft in those days. The spell of a witch was thought to bring about all manner of ills to man and beast. Witch hunts were carried out to rid communities of those who were "possessed," as persons dangerous to the health of a community. The witch scare eventually subsided, but to this day the idea prevails to a certain extent that extrinsic influences can bring about congenital deformities.

The medical profession has been searching for intrinsic causes for these calamities in the newborn. Of late it has been shown that certain characteristics and congenital anomalies are derived from the genes. These include blood-group antigens, hemophilia and several other conditions,[65] and animal experiments have shown that a lack of vitamin A early in pregnancy can bring about cataract.[66, 67] It now appears that prenatal infection can so disturb the development of the eye and other organs of the body as to cause gross deformities. The Flibbertigibbet of today responsible for at least some congenital defects seems to be the virus of rubella, which stalks unseen by day as well as by night in the house, the schoolroom and crowded places and which until recently was quite unsuspected and unfeared.

Miscarriage and Stillbirth

An obstetrician, Dr. Raymond B. Titus, asked me to see a primipara with a typical attack of rubella in the third month of pregnancy. The attack appeared to pass off in an uneventful manner. Six months later Dr. Burnet, of Australia, informed me of the dangers of rubella to the fetus. From Dr. Titus I learned that the patient had subsequently miscarried. At about that time a twenty-three-year-old primipara was admitted to my service at the Haynes Memorial with rubella. She miscarried on the sixth hospital day. Through the courtesy of Drs. Dwight L. Siscoe and C. J. Dunlop I learned of a patient who suffered an attack of rubella in the first half of the second month of pregnancy. Quickening was recognized after the fourth month and then ceased to be present. With failure of the uterus to increase in size the death of the fetus was determined. A macerated fetus was delivered in the seventh month. The mother has since been delivered of a healthy infant. A miscarriage in the third month of pregnancy after an attack of rubella in the second month has been reported by Swan and Tostevin.[68] On examination of the fetus a unilateral cataract was found. Goar and Potts[69] describe twins at seven months from a mother who had rubella in the first month of pregnancy. One was stillborn, and the other twin lived but had bilateral cataracts and a congenital heart lesion. A stillbirth with hydrocephalus in the seventh month of pregnancy following an attack of rubella in the first month has been reported by Fox and Bortin.[70] These authors, however, present another side of the picture, reporting normal twins and 2 other normal babies born of mothers who had rubella in the second month of pregnancy, 3 normal infants of mothers who had rubella in the third month, 1 normal baby whose mother had rubella in the fourth month and 2 normal babies from mothers who had rubella in the seventh and ninth months. All the normal infants were born at full term.

Thus, following an attack of rubella, the mother may miscarry, may be delivered of a premature stillborn child with deformities, may be delivered of a living child with serious congenital deformities or may go to full term and give birth to a perfectly normal child.

A more serious virus disease, smallpox, is known to cause miscarriage, and some French authors[42] have found this to occur in 50 to 60 per cent of cases. In relapsing fever, which is a rickettsial disease, a fetal mortality of 92.4 per cent has been recorded.[71] It is possible that the lower virulence of the rubella virus enables the fetus to survive more frequently, but such a survival may lead to the birth of a child

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with gross congenital deformities. This relatively low virulence in mortality of the fetus becomes a greater calamity through a relatively high morbidity with subsequent serious defects.

Congenital Anomalies

In 1941 Gregg[1] reported a series of 78 cases of congenital cataract in which 13 patients were seen in his own practice. A definite history of rubella during pregnancy was obtained in 68 cases, and in the remaining 10 there was a suspicious history of rubella, although a definite diagnosis could not be established. Forty-four children presented evidence of congenital heart lesions, and patent ductus arteriosus was shown at autopsy in 3 cases. A characteristic of many of these infants was that they were poorly nourished and presented difficult feeding problems. This discovery by Gregg resulted from his correlating the finding of so many congenital cataracts with the fact that a rubella epidemic of unusual proportions had been in progress in Australia in the preceding year. In looking backward for an antenatal explanation he found that this relatively minor exanthematous disease had been an almost consistent factor during pregnancy.

Under the direction of the National and Medical Research Council of Australia a survey was instituted under the direction of Swan and his associates[72] in South Australia. Their report on 61 children, covering the period from 1939 to 1942, inclusive, revealed that 49 mothers who had suffered an attack of rubella during pregnancy gave birth to 31 infants with congenital defects. Among the mothers of these defective children, 29 had had rubella in the first three months of pregnancy, and the 25 who had had the disease in the first two months of pregnancy gave birth to infants with congenital defects. Four of the 8 mothers who had had rubella in the third month gave birth to congenitally defective infants. Two defective children were born of mothers who had had rubella after the third month. As opposed to the 31 defective children 18 healthy children were born of these 49 mothers. Four cases of congenital cataract were found in which the mother denied any history of an exanthem during pregnancy. The relation between the month in which rubella was contracted and the occurrence of congenital defects is demonstrated in Table 1.

As in the Gregg report the majority of the children were poorly developed and presented feeding problems. In this series, however, the cardiac defects predominated: there were 17 infants with heart lesions, and 14 with eye defects. Seven were deaf mutes, and 4 showed mental retardation. The defects frequently appeared in combination. Among the 17 patients exhibiting cardiac lesions there were 8 who also had cataracts and 2 who were also deaf mutes. These striking combinations were revealed in later reports and constitute the suggestion of a syndrome of rubella effects.

Further reports from Australia by Swan and his associates,[73, 74] Gregg and his co-workers,[75] Evans,[76] Carruthers,[77] Welch[78] and Vickery[79] strengthened the conviction that rubella was an etiologic agent of prime importance in these congenital deformities.

Evans[76] investigated the dental abnormalities among the first group of children reported by Swan and his associates.[72] In 34 infants whose mothers had had rubella during pregnancy there were 18 with dental defects of a major character, consisting of marked retardation of tooth eruptions, defective formation of the incisors and hypoplasia.

Table 1. *Relation between the Time of Contraction of Rubella during Pregnancy and the Occurrence of Congenital Defects.*[72]

Stage of Pregnancy	No. of Infants with Congenital Defects	No. of Healthy Children	Total
0 to 1	8	—	8
1 to 2	17	—	17
2 to 3	4	4	8
3 to 4	1	2	3
4 to 5	—	3	3
5 to 6	1	3	4
6 to 7	—	3	3
7 to 8	—	1	1
8 to 9	—	2	2
Totals	31	18	49

Carruthers[77] examined 17 of the cases of deafness found in the survey made by Gregg et al.[75] in New South Wales. The severity of the attack of rubella appeared to have no relation to the severity of damage in the ear. Most of the children gave some evidence of hearing over the tone range from 512 to 2048. Nine patients were given caloric labyrinthine tests with results that showed little deviation from the normal except that there was no vomiting even though nystagmus was induced. Post-mortem examination of one infant who died at the age of six and a half months and whose mother had suffered an attack of rubella in the first month of pregnancy disclosed underdevelopment, congenital cataracts and a patent ductus arteriosus. The ossicles of the middle ear were normal, but in both ears there was a total lack of differentiation of the primitive cells in the organ of Corti. Welch[78] supplied another study from New South Wales, covering 34 cases of congenital deafness in children born in 1938 to mothers who had had rubella in pregnancy. All these cases showed islands of deafness in the tone range.

From the pediatric point of view Vickery[79] studied the children of 20 mothers who had had rubella in the first three months of pregnancy. All were partially deaf and backward in speaking. Eleven were undersized and underweight. All infants presented problems in management, with sleeplessness and nervous irritability. Only 2 had congenital

cataracts, but 13 showed cardiac lesions with murmurs, precordial bulging and, on x-ray examination, left ventricular dilatations. In 1 case the ductus arteriosus was successfully ligated by operation.

A survey made by Gregg and his co-workers[75] revealed that the reported cases of rubella in school children in New South Wales from 1933 to 1943 showed a substantial rise to 1000 cases in 1936 and to 4683 in 1937. There was a sharp rise to 30,228 cases in 1940, and during that year 116 women were known to have contracted rubella in pregnancy, although the actual number is unknown. To these 116 women 117 babies were born, of whom 78 showed deaf mutism, 15 deaf mutism and heart disease, 4 eye disease, 4 eye and heart disease, 4 heart disease, and 6 deaf mutism and eye and heart disease. All these defects occurred in infants whose mothers had contracted rubella in the first four months of pregnancy, except for 8 cases in which the time of the attack was undetermined. The great majority of the defects occurred in cases in which the attacks had occurred in the first three months. In 1940 only 5 normal babies were found whose mothers had had rubella in pregnancy. The rubella occurred in the third month in 1 case, the fourth month in 1, the fifth month in 2 and the seventh month in 1. Two of the 116 mothers gave a history of an attack of rubella previous to the one in pregnancy. In addition, 20 cases from other years were included in this report, giving a total of 136 cases.

TABLE 2. *Relation between Stage of Pregnancy at Onset of Rubella and Birth of Defective and Normal Children (Based on Australian Survey*[68, 73-75]).

Stage of Pregnancy	Infants with Congenital Defects		Normal Children		Total
mo.					
0 to 1	30		2		32
1 to 2	88		2		90
	—		—		
First 2 months		118		4	
2 to 3	59		5		64
First trimester		177		9	
3 to 4	28		4		32
4 to 5	3		5		8
5 to 6	2		7		9
Second trimester		33		16	
6 to 7	—		4		4
7 to 8	1		2		3
8 to 9	—		2		2
Last 5 months		6		20	
Third trimester	—	1	—	8	—
Totals	211		33		244

It will be observed that these Australian investigators have delved into the subject from many different angles. The question was raised whether this Australian epidemic was due to some mixed infection. A severe sore throat had been prevalent in Australia, but Swan and his associates[72] showed that cultures yielded a predominance of *Haemophilus influenzae*. Furthermore, no correlation between the sore throats and the congenital defects could be established. Thus, a mixed infection with symbiosis was eliminated. Next, the possibility of an unusual strain of rubella virus was considered. It must be kept in mind that this epidemic of 1940 took place during a war year, with troop mobilization in progress. It is well known that many diseases show acceleration in morbidity during military mobilization, and with such acceleration the virulence of the etiologic agent is often increased. Several of these authors remarked on the severity of the rubella attacks and the frequency of rheumatic sequelae. Nevertheless, the incidence and severity of the congenital deformities bore no relation to the severity of the attacks in the mother. Furthermore, reports from England[24] and the British Expeditionary Forces[87] described epidemic rubella with characteristics of similar severity at the same time. A survey made by Prendergast[80] of congenital deformities following maternal rubella in California yielded results similar to those reported from Australia, and it was suggested that the Australian strain had been introduced into California because of the close communication between the west coast of America and Australia during the previous five years. It appears that here again an accelerated morbidity due to intensive military mobilization was involved, during which an increased number of pregnant women contracted rubella early in pregnancy; as a result, 40 infants were found to have gross congenital deformities as against 4 normal babies whose mothers had contracted rubella in the first trimester of pregnancy. There seems to be no valid reason for supposing that the virus of rubella during epidemic conditions acquires any augmented powers of invading the fetus in utero. Epidemics merely offer the virus an increased opportunity to attack pregnant mothers. The Australian epidemic was of sufficient proportions to lead Gregg to his discovery of the causal relation of rubella to the congenital cataracts that came under his care.

The various reports from Australia come from independent investigations and surveys. Some of the investigations conducted by specialists deal with cases studied in the surveys. The work of Carruthers[77] on deafness was carried out on the cases covered in Gregg's[75] survey, and the actual number of cases with deafness was found to be greater than that in the survey. It is impossible, however, to include these additions in the survey figures. On the other hand, the studies of Evans[76] on the dental defects of the patient in the survey of Swan et al.[72] can be incorporated under the survey without reduplication in the number of defects found in this group.

Each author or group of authors have studied the subject either from the point of view of a survey or according to the specialty of the author. There has been a decided lack of any attempt to unify the results. Table 2 presents the figures of

the various surveys of Swan, Gregg and their many associates. This compilation deals with the relation of the time of contraction of rubella during pregnancy and the birth of defective and normal children. It will be seen that in general this conforms with Table 1. The results are startling. When rubella occurred in the first two months of pregnancy there were 118 infants with congenital defects and only 4 normal ones, whereas when the attack of rubella took place in the last five months of pregnancy there were 6 babies with congenital defects and 20 normal ones. This indicates that during the surveys. None of these, however, compare with the figures supplied from Australia. Nevertheless, the combined results add greatly to the evidence that rubella in the early months of pregnancy is a serious problem.

The subject of the normal babies born of mothers who contracted rubella during pregnancy seemed to be worthy of further investigation. I have therefore assembled these in Table 3, combining the figures already utilized in Table 2 with those derived from America, giving a total of 48 normal infants. The figures are again arranged by months

TABLE 3. *Normal Babies Born to Mothers Who Had Contracted Rubella during Pregnancy.*

AUTHOR	MONTH OF PREGNANCY									TOTAL
	0–1	*1–2*	*2–3*	*3–4*	*4–5*	*5–6*	*6–7*	*7–8*	*8–9*	
Swan et al.[72]			4	2	3	3	3	1	2	18
Swan et al.[73]						2				2
Swan et al.[44]		1		1		1				3
Swan et al.[74]*	1	1				1		1		4
Gregg et al.[75]	1		1	1	2		1			6
Fox and Bortin[70]		4	3	1			1		1	10
Councilman†								1		1
Conte et al.[51]								1		1
Aycock and Ingalls[59]		1		1					1	3
Totals	2	7	8	6	5	7	5	4	4	48
Prendergast[80]‡			4							
First trimester			17							
				21						
Second trimester			18							
Third trimester			13							
Total				52						

*Includes infants with umbilical hernia and strabismus.

†Personal communication.

‡Figure supplied by obstetricians of California in answer to a questionnaire that concerned rubella only in the first three months of pregnancy.

first two months of the life of the fetus there is an extraordinary vulnerability of certain tissues to the virus of rubella. This is less marked in the third month, with a ratio of 59:5, and in the fourth month, with a ratio of 28:4, and diminishes in the subsequent months of pregnancy.

It has been the custom to discuss these figures according to the trimester of pregnancy. The figures arranged in this manner do not give the startling results of the comparison of the first two months with the last five months because of the relatively small number of normal infants born to mothers who had had rubella in the last trimester. One would expect a much larger number, because in a consideration of the vulnerability of the fetus by trimesters, the ratio of normal babies should increase in inverse proportion to the number born with congenital defects. This is not apparent, and therefore it fails to confirm the startling figures of the first two months in comparison with those of the last five months.

Numerous reports have appeared from the United States and England. It is impossible to do justice to the detailed studies that have been made. With the exception of the survey by Fox and Bortin[70] in Milwaukee these reports confirm the findings in Australia. Some are simply isolated reports dealing with single cases, whereas others are valuable as well as by trimesters. From these it is observed that 9 normal babies were found whose mothers had had rubella in the first two months of pregnancy as against 25 in the last five months. But if the entire period of nine months is divided into the three trimesters the figures are 17, 18 and 13 respectively. Here again, there is no inverse ratio of normal children to those with congenital deformities. The addition of Prendergast's[80] cases is necessary but confusing because the questionnaire sent out to the physicians in California asked only for information regarding babies born to mothers who had suffered rubella in the first trimester. The figures in Table 3, with the exception of the first month with 2 normal babies, lends no support to the figures of congenital deformities, which are strongly indicative of the vulnerability of the fetus in the early months of pregnancy. Indeed, these figures on normal babies tend to sustain the results obtained by Fox and Bortin.[70] If it is considered, however, that in the past five years there have been reports of only 52 normal babies born of women who had contracted rubella during pregnancy and that only 2 cases have been reported in which the mother had rubella in the first month of pregnancy, the negative evidence supplied in Table 3 and in the survey of Fox and Bortin fades before the overwhelming evidence against rubella. Especially is

this apparent when the combined figures assembled from the literature of Australia, the United States and England yield reports of 521 children born with serious congenital deformities during the past five years following maternal rubella. This is a ratio of ten grossly deformed children to one normal child, irrespective of the month in which rubella was contracted.

The details regarding these 521 congenitally deformed children are presented in Table 4. It will be seen that 359 of the cases occurred in Australia, 110 in the United States and 52 in England. The further details are incomplete because many of the patients were examined by specialists in their respective fields, — for example, for eye or ear defects alone, — and some of these infants did not live long enough to reveal deafness, mental retardation or dental deformities. Among these children there were 221 with eye defects, 243 with deafness, 221 with heart lesions, 74 with microcephalus, 24 with mental retardation, and 20 with gross dental deformities. Actually, mental retardation was far more frequent than these figures indicate, since in numerous reports the statement is made that in "many" or "most" of the cases this defect was apparent. Often this was difficult to ascertain because of the existence of deafness or blindness, or both. Furthermore, it is futile to attempt to show the combination of these deformities, since this has already been emphasized. I have left out several other deformities noted occasionally, such as an arachnodactyly, which is clearly hereditary, and cleft palate, which can be brought about by environmental modifications as well as by genetic mutations.[82] There were 3 cases of pyloric stenosis, 2 of obliteration of the bile ducts, and 1 of spina bifida. These were all found in conjunction with the other deformities characteristic of infants born of mothers who have had rubella. That there were 3 cases of pyloric stenosis is of significance because the finding of these defects among the 521 cases constitutes a high incidence.

It is interesting to note that in the survey made in Tennessee by Conte, McCammon and Christie[81] it was estimated that the rate of babies with congenital anomalies born of mothers who had had rubella in pregnancy was ten times greater than that for congenitally deformed babies in the population at large.

The finding of these congenital deformities following maternal rubella has naturally aroused interest in the possibility that other infectious diseases, particularly those of virus origin, will cause similar defects. In this respect the Australian investigators, Gregg and Swan with their respective associates, have shown particular interest. Deaf mutism, patent ductus arteriosus, microcephalus and pyloric stenosis have been recorded following

TABLE 4. *Severe Congenital Deformities among Children following Rubella in Pregnancy.*

PLACE	YEAR OF PUBLICATION	AUTHOR	TOTAL NO. OF CASES	EYE DEFECTS	DEAFNESS	HEART LESIONS	MICROCEPHALUS	MENTAL RETARDATION	DENTAL DEFECTS	PYLORIC STENOSIS
Australia	1941	Gregg[1]	78*	78		44				
Australia	1945	Gregg et al.[78]	136	23	85	38	44			
Australia	1943	Swan et al.[78]	31	14	7	17	3			
Australia	1944	Swan et al.[79]	12	2	5	4				
Australia	1946	Swan and Tostevin[83]	36	1	22	19	18			2
Australia	1946	Swan et al.[74]	12	1	6	8		1		
Australia	1944	Evans[75]							18	
Australia	1945	Vickery[76]	20	2	20	13				
Australia	1945	Welch[84]	34		34					
New York	1944	Reese[85]	3	3		1				
Pasadena, California	1944	Erickson[86]	11	11		9		2		
Washington, D. C.	1944	Rones[88]	3	3						
New York	1945	Perera[25]	1	1		1				
Milwaukee, Wisconsin	1945	Greenthal[87]	2	1	1	1		1		
Spokane, Washington	1945	de Roetth and Greene[89]	2	2		1	1			
Los Angeles	1945	Albaugh[90]	9	8		8	5			1
Minneapolis	1945	Adams[91]	2	2		2				
Nashville, Tennessee	1945	Conte et al.[81]	5	4		4	1	4		
New York	1945	Altmann and Dingmann[81]	1	1	1					
Chicago	1945	Krause[92]	5	5	1	3		3		
California	1946	Prendergast[93]†	40‡	40		27		3		
Colorado	1945	Long and Danielson[82]	6	6		6				
Richmond, Virginia	1946	Guerry[94]	2	2		1		1		
Houston, Texas	1946	Goar and Potts[95]	6	6		5		2		
Massachusetts	1946	Aycock and Ingalls[29]	1					1		
Massachusetts	1946	Hopkins[35]	11	2	11	3		6		
England	1944	Simpson[24]	2	2		2				
England	1945	Hughes[80]	1	1	1	1	1			
England	1945	Mavitin[77]	30‡		30	3				
England	1947	Clayton-Jones[96]	19		19		1		2	
Totals			521	221	243	221	74	24	20	3

*In 10 of these cases the diagnosis was suspected but not definitely established.
Since the studies of Carruthers on deaf mutes were done in cases included in the series of Gregg[1] and the Evans studies on dental defects were done in the series of Swan et al.,[78] which are summarized in the text, these reports are omitted.

†Most conservative use of figures given in order to avoid reduplication in reports of 80 cases from the State.

‡Diagnosis of rubella probable in 6 cases. Total number of probable diagnoses in this table is 22. Cases given as possible diagnoses have been omitted.

such diseases as measles,[72, 85] mumps, chicken pox and herpes zoster[68, 72] and influenza.[72, 95] There is nothing as yet in the literature, however, to suggest that such diseases — with the possible exception of influenza[74] — compare with rubella in bringing about these congenital deformities, much less a syndrome of eye, ear and heart defects. It is important to remember that these deformities may occur without any history of rubella. Fox and Bortin[70] described a woman who in 1937, after a supposedly uneventful pregnancy, gave birth to an infant with bilateral cataracts; in 1945 she is said to have had rubella in the second month of pregnancy, after which she gave birth to a normal infant. From my hospital experience I am aware of so many cases erroneously diagnosed as rubella that I cannot be too sure of the accuracy of the state reports on this disease. The environmental influence of other infections on the fetus in utero needs the same concerted investigation that is being given to rubella.

It must be kept in mind that these reports and surveys represent a backward approach to the problem. As such, there is much that is unsatisfactory from an investigative point of view. Although rubella is a reportable disease, it is often not reported, and as I have intimated above, it is frequently improperly diagnosed. Any backward approach through cases reported to boards of health must take into consideration these possible errors of omission and commission. Eventually, we shall have a series of pregnant mothers who have unquestionable rubella and are followed through, the incidence of miscarriages, stillbirths and the findings at autopsy, as well as of normal children and those born with congenital defects, along with the full details of such defects, being given. Similar investigations must also be undertaken through the entire field of infectious diseases so that the position of rubella in this respect can be properly ascertained. Until adequate studies have been carried out in this manner opinion must be based on such evidence as can be gathered by this backward method of surveys of rubella and of congenitally deformed children.

To date the available evidence points to a 10:1 chance (521:52) that a woman who has rubella in pregnancy will give birth to a child with a gross congenital deformity, such as cataracts, deaf mutism, patent ductus arteriosus or mental retardation, and not infrequently with a combination of these defects. The incidence of the deformities is in inverse proportion to the month of pregnancy in which the attack of rubella takes place. Thus, the likelihood that such a deformity will follow rubella in the first and second months is the greatest. It was first estimated at 100 per cent by Australian authors (Table 1). Later this was modified to 118 to 4 by our compilation of Australian surveys (Table 2). Utilizing the figures on normal babies (Table 3) alone, I should lower the estimate still more, but the mass of evidence points to a serious and startling proportion of deformities — well above 10:1. This ratio changes with each month of pregnancy, and the danger of giving birth to a deformed child decreases to the zero point in the last month (Table 2). In the California survey of the first trimester only, the most conservative estimate was 40 deformed and 4 normal babies.[80] From the Tennessee survey it was estimated by a rather roundabout method that the proportion of deformed children born to mothers who had rubella is ten times greater than the congenitally deformed children born of the population at large.[81]

Against all this mass of testimony are the results of the survey made in Milwaukee by Fox and Bortin.[70] This report deals with 12 babies born of mothers who had rubella during pregnancy, in 8 of whom the attack of rubella had occurred in the first three months. Seven normal babies were born, including a pair of twins. There was one stillbirth at the eighth month, and one "blue baby" with hydrocephalus, who subsequently became normal. Of course these results differ from those in all the other surveys. On careful analysis, however, one cannot agree with the conclusions of these authors, which imply that rubella presents no serious danger to the fetus. Two of the children came very near to being badly deformed. One died in utero late in pregnancy as stillbirth with hydrocephalus. Had it lived the child would in all probability have been a mental defective. The other was a "blue baby" with hydrocephalus who subsequently recovered and became "perfectly normal." There were, therefore, two very fortunate escapes among these 8 children, and this signifies a serious hazard in those 2. If the 6 cases in which rubella occurred in the first two months of pregnancy are considered, it might be stated that 2 of the 6 children barely escaped becoming seriously deformed. These normal infants studied by Fox and Bortin are included in Table 3 to give the figure of 52 normal babies as a balance against the collected 521 grossly deformed children, giving a ratio for all months of pregnancy of one normal child against ten grossly deformed children — a formidable indictment against rubella and one deserving of special consideration under the treatment of this disease. Added to this is the conspicuous demonstration that most of the deformities followed an attack of rubella in the early months of pregnancy. Consequently, there appears to be little room for doubt regarding the serious danger of this disease to the fetus during the early months of gestation. The evidence at hand, although unsatisfactory in several ways, is sufficient to warrant consideration in the management of this problem.

Congenital Deformities Following Attacks of Rubella before Conception

A curious phenomenon that has come to light is difficult to explain in a disease of such short duration as rubella. Hall[99] reports the case of a child

born in 1942 with a congenital heart lesion, bilateral cataracts and complete deaf mutism, whose mother is said to have suffered a "sharp attack" of rubella six weeks before conception. Sweet[100] supplies the report of a woman who contracted rubella ten days before conception, the date of conception being fixed by the husband's three-day military leave. This pregnancy resulted in the birth of an infant that had bilateral cataracts, patent ductus arteriosus and hydrocephalus and lived only three months. The mother has since given birth to a perfectly normal child. In contrast are the 2 cases reported by Swan and Tostevin[98] in which rubella was contracted thirteen days and six days, respectively, before conception. This was figured out on the assumption that "ovulation occurs approximately fourteen days before the onset of the next menstrual cycle and that fertilization takes place within twenty-four to forty-eight hours of ovulation." It is interesting that in the first case a therapeutic abortion was carried out in view of the possibility that the child would be malformed. The specimen sent to the pathological laboratory consisted of fragments of tissue. Both eyes were intact, and further histopathological examination revealed no abnormality. The other patient went to term, and the child was normal.

Treatment

Aside from the problem of rubella in pregnancy, this disease is so relatively mild in the vast majority of cases that the natural recuperative powers of the body need no special help from the armamentarium of the physician. If fever is present bed rest appears to be indicated, unless the new notion of getting sick people out of bed captures the fancy of the modern doctor. Certainly, bed rest need not be enforced too strictly. One has but to be reminded that in another virus disease — namely, mumps — it has been clearly shown that the old notion of strict bed rest does not diminish the incidence of orchitis. It is highly improbable that complete rest in bed will diminish the rare complications of rubella. Most of the patients with mild cases do not stay in bed anyway and do perfectly well if they are permitted to be up and about. I had the opportunity of observing an epidemic of rubella in a regiment in a training area. The first 2 patients were admitted to a measles ward. After this affront, with the connivance of two superior officers, the subsequent patients remained on full duty. Those who were sick remained in quarters. The epidemic burned itself out without any sequelae other than a threatened court martial, which never materialized. This method of dealing with epidemics of rubella has been successfully carried out in lay institutions. During the Blitz in London, sadly needed beds for casualties were occupied by patients with rubella.

In 1814, when blood letting was in vogue, Maton[6] gave due consideration to this form of therapy, deeming it unnecessary in cases of rubella. He advocated nothing more than purgation. Paterson,[7] in 1840, favored the fad of his day, recommending the application of leeches to the chin and sternum, as well as enough wine of colchicum to induce vomiting and purging. If constipation is present it needs gentle correction. A reasonable amount of activity of the skeletal muscles tends to avoid this condition and is preferable to overactivity of the smooth muscles of the entire gastrointestinal tract. If the eruption is accompanied by itching, which is rare, calamine lotion is indicated. Some physicians have found warm baths helpful. A little activity takes the mind off this minor disturbance. A good night's sleep can be achieved in a quiet environment without the aid of a narcotic. Gargles and nose drops are quite unnecessary.

It goes without saying that sulfonamides and penicillin are not indicated, and yet I have seen both generously applied, according to the spirit of the times, before the patient was admitted to the hospital. This is a pure waste of valuable medicines. The same thing could be said of the vitamins; there appears to be ample vitamin reserve to carry a patient through an attack of this disease. As a matter of fact, no one has the slightest idea of the relation of vitamins to resistance to rubella. Serum therapy is quite unnecessary for the ordinary case. Jacob Bigelow's[101] address, "On Self-Limited Diseases," delivered before the Massachusetts Medical Society in 1835, is still good prescribed reading. In short, there is little that need be done except to make the patient comfortable, and since in the vast majority of cases the patient suffers not so much from discomfort as from the deprivation of his usual pursuits and activities, the possible advantages and disadvantages of imposing restrictions should be carefully considered. Before the recognition of the deleterious effects of rubella on the fetus in utero there was a growing tendency in various boards of health to remove all isolation requirements. In view of the newer knowledge of this disease this idea needs reconsideration. The treatment of the pregnant woman who suffers an attack of rubella is discussed below.

Prevention

Protection against rubella is like protection against an atom bomb, and can be summed up in one word — distance. If exposure could be avoided, the disease itself could, of course, be prevented. On the other hand, exposure to the disease in childhood appears to be advantageous, since an attack is likely to afford a lifelong immunity. Therefore, the proposition that it is advisable to have rubella in childhood advances the corollary that it is advisable for all children to be thoroughly exposed, which means the removal of all isolation precautions, so that as many children as possible can have the disease and thereby acquire immunity from sub-

sequent attacks. The fallacy in such a sweeping statement lies in the fact that many children in the community have mothers who are pregnant and who may or may not have had rubella — many mothers are ignorant of whether or not they have had it. It has already been pointed out that the immunity from one attack is not always permanent; it is only relatively permanent. Thus, the removal of precautionary isolation may entail the danger of rubella in pregnant mothers contracted from children exposed in kindergarten or school. Certainly, this contingency is to be avoided if possible, but it presents one of the most difficult problems. It is easy enough to say that all children should be inoculated with the virus of rubella, but an active virus would give rise to the disease itself, which would be communicable to others. Therefore, although it is safe to say that an epidemic of rubella should be allowed to run its course in asylums and boarding schools and in such colleges as can be isolated for the time being, the same statement cannot be postulated for day nurseries, kindergartens and day schools or colleges situated in metropolitan centers.

It has been pointed out above that this disease appears to be communicable just prior to the eruption and that communicability diminishes abruptly with the disappearance of the rash. Consequently, since the rash is of short duration, isolation for the eruptive period is effective for only about half the period of infectivity. Thus, the factor of time must also be considered in relation to distance in the matter of exposure.

Barenberg and his co-workers[102] have offered presumptive evidence that the intramuscular injection of pooled serum or plasma will prevent rubella in children. The duration of such protection is unknown. This method could be utilized in children exposed to rubella whose mothers are pregnant. At the same time, larger doses could also be injected into the pregnant mothers. Just how reliable such an attempt at affording passive immunity would be in the event of a protracted epidemic, even though repeated doses were given, remains to be determined. One must take into consideration the possibility that such a serum will be contaminated with infectious hepatitis. Gamma globulin, which has been proved to be effective after exposure to measles and ineffective after exposure to chicken pox, is as yet an untried weapon against rubella. Until a vaccine of modified rubella virus that will not give rise to a communicable form of the disease and yet will afford a permanent immunity has been perfected, the complicated problem of protecting pregnant mothers from contracting rubella will remain.

Treatment of the Pregnant Mother Who Contracts Rubella

It would be interesting to know whether pregnancy renders a woman more susceptible to rubella. Apparently, the manifestations of rubella in the pregnant woman are no severer than those in other persons; thus, there is no real direct danger from the virus to the mother herself. Once exposure has taken place and the incubation period has passed and the rubella eruption has reached the stage where the disease can be recognized, there is the possibility — in the early weeks of pregnancy, the probability — that the virus has gained access to the fetus. Evidence has been presented pointing to the susceptibility, which is particularly marked in the first two months of life, of certain fetal tissues to the virus of rubella. This premise presupposes that the virus would attack the fetal tissues as soon as it became active in the mother, if not sooner. If the virus has already combined with these fetal structures the question arises whether any number of protective antibodies contained in antiserums administered to the mother would preclude serious damage to the fetus. By the time the disease is recognizable in the mother it is highly probable that the virus would already have accomplished serious injury to the more susceptible embryonic tissues, and that no amount of antiserum could offset the damage. The administration of such an antiserum in any of its present forms would leave one with the uncertainty of its efficacy.

Threatened Miscarriage

Whether or not antiserum has been administered, any signs of miscarriage ought to be welcomed, and I can see no justifiable reason for any attempts to avoid such a favorable event. There is nothing in the dictates of the medical profession or in the common law of English-speaking countries that instructs a physician to attempt to prevent a miscarriage in the face of the evidence that has been presented. To bring up the religious motive of preserving life at all costs is on a par with the superstition of the Hindu who will not kill a cobra that attacks his own child because the cobra is a sacred animal.

Of course, a human life is sacred. Yet, under certain circumstances, one may take a human life in self-defense, both in peace and in war. A nation at war expends the lives of its citizens. Physicians are not bound to preserve life at all costs. Nothing is gained by saving a life when agony and anguish lie ahead, whether in the death throes of cancer or in the future birth of a grossly deformed infant. Because human life is sacred, there are exceptions to preserving it at all costs and under all circumstances. Physicians are now faced with a new exception. No attempt should be made to prevent a threatened miscarriage in the course of or after an attack of rubella, especially when the disease occurs in the early months. It is entirely up to the judgment of the attending physician to bring this to completion by surgical means. The medical profession is engaged in the prevention of disease, the preservation

of life and the amelioration of suffering. The immediate problem does not come under the much discussed topic of legalizing euthanasia, which has to do with that praiseworthy function of making impending death comfortable. The problem presented by rubella in pregnancy deals with the prevention of suffering in its broadest sense.

Therapeutic Abortion and Its Medicolegal Aspects

The instigation of a therapeutic abortion is quite a different matter from allowing a threatened miscarriage to proceed and bringing it to completion by surgical means. The suggestion of terminating pregnancy after an attack of rubella was first introduced by Swan and his associates.[72] In a subsequent article it was made clear that no legal grounds existed in Australia for the termination of pregnancy after rubella.[72] Furthermore, they gave as their expressed opinion that legislation to such an end might lead to its abuse. Albaugh[89] and Lynch,[103] in America, and Hughes,[96] in England, have urged that caution be used in the consideration of abortion. Fox and Bortin[70] found in the results of their Milwaukee investigations no justification for considering the termination of pregnancy. When one contemplates the mass of cumulated factual evidence presented in this paper the idea of therapeutic abortion cannot be pushed aside. Such abortions in 3 cases have already been reported in the medical literature.[74, 104]

In dealing with a diseased patient the physician uses every effort to remove all obstacles in the way of recovery. The word "recovery" must be construed to include the aftereffects of the disease. If a woman suffers an attack of rubella during the first months of pregnancy, the chances of her giving birth to a grossly deformed child are sufficient to warrant an abortion from the purely medical point of view to ensure complete recovery from the aftereffects of the disease. The law forbids physicians to perform an operation for that purpose.

According to the common law and the statutes in some states, it is illegal to terminate pregnancy except to save the life of the mother. For instance, therapeutic abortion is permitted in the case of a pregnant woman suffering from tuberculosis. This is done for the safety of the expectant mother. The consultation of a second physician — and usually the permission of the executive committee of the hospital — is required. After an attack of rubella the life of the mother is usually not endangered by a grossly deformed living fetus; only if the fetus develops a massive hydrocephalus can the life of the mother be said to be threatened. This is a relatively minimal danger. Nevertheless, such a possibility exists, even though remote, and could be seized on as a point in law; and possibilities are being dealt with. The woman with tuberculosis does not always succumb from carrying a child, but she is likely to do so. An attack of rubella in the early months of pregnancy does not always result in serious malformations in the fetus, but it may do so. Such a possibility weighs heavily on the minds of the attending physician and the parents.

The purpose of terminating pregnancy is to prevent the birth of a deformed infant and to allow the mother to conceive again under more auspicious circumstances. The desire to accomplish this is irrelevant in the eyes of the law. From the legal point of view this desire is prompted by social reasons, which are not acceptable as valid grounds for abortion. These grounds are actually far more valid than the grounds in which abortion is usually sought, because the birth of a deformed child acts as a deterrent to future pregnancies. The birth of a deformed child as a result of rubella in no way prevents the future birth of normal babies. Nevertheless, in Australia, investigations showed that mothers of infants deformed by rubella refrained from having more children because of the fear of giving birth to another defective child or because the care of the defective child precluded their having any more children.[74]

If the fetus dies the uterus may be emptied. There is no question here of destroying life. Consequently, the determination of a dead fetus warrants emptying of the uterus. It can always be argued that the presence of a macerated fetus could serve as a nidus for the Welch bacillus, so frequently inhabiting the intestinal tract of normal persons. Such a possibility, however, is remote. Ordinarily, a dead fetus offers no particular danger to the mother. The real question is how to determine the presence of a dead fetus in the early months of pregnancy. Failure of the uterus to grow is, of course, an indication that the fetus is dead. Consequently, if the attending obstetrician decides that the fetus is not living, he may empty the uterus. A consultation is indicated, to share responsibility, and the written permission of the expectant mother, as well as of the husband, should be obtained. Although the common law permits emptying of the uterus when the fetus is dead, the statutes on this whole subject vary in different states — for example, in Massachusetts, Maine, New York and Iowa.

The fundamental law regarding abortion lies in the Offense against the Persons Act of England. Any approach to this law as it relates to the pregnant woman who suffers an attack of rubella must be made with two possibilities in mind. The first, which has to do with a favorable interpretation of this law and the statutes that pertain to it, would permit an exception under these circumstances. The second, which concerns a change in the statutes, would grant permission to carry out abortion under the explicit circumstance of an attack of rubella. It is my purpose to show that a favorable interpretation has been rendered in relation to this subject in a court of law, and to bring out a pertinent bit of history regarding a law that was entirely changed.

The present status of the law regarding abortion in reference to rubella has been reviewed in an editorial in the *Lancet*. It is pointed out that abortion is a statutory felony under the Offense against the Persons Act. A later proviso was introduced as an amendment whereby no person should be guilty under this section if the act "was done in good faith for the purpose only of preserving the life of the mother." In 1938 Mr. Justice Macnaghten, in charging a jury, suggested that this clause did not mean that the surgeon operates only if the life of the mother is in immediate danger. It was his opinion that this section of the law construed "reasonably" would protect the surgeon if in his best judgment the continuation of pregnancy would have led to the patient's becoming "a physical and mental wreck." The editorial continues as follows: "If a woman can be assured that her child is certain to be born with some terrible deficiency, it might well have the same effect." Actually, there is no more assurance that the child will be born with gross deformities as the result of rubella than there is that the woman with tuberculosis will die if allowed to continue her pregnancy. Nevertheless, if a woman is aware of the statistical evidence in her particular case regarding the period in her pregnancy when the attack of rubella took place, there can be no doubt that she would become "a mental and physical wreck" if the pregnancy were allowed to continue. Indeed, it could be said that in the end it might endanger her health as much as an attack of tuberculosis. Justice Macnaghten's opinion was rendered before anything was known of the dangers of rubella during pregnancy. A liberal interpretation of the law based on his construction would depend on the court and the sympathy of the jury. A closer interpretation of the law would stress the fact that the mother's life was not endangered by the attack of rubella, and that the surgical termination of pregnancy under such circumstances is therefore a felony. It is necessary to point out that conviction of such a felony brings a severe penalty, with fine, imprisonment and the loss of license to practice.

It was pointed out above that congenital deformities were at one time attributed to a witch casting a spell on a pregnant woman. Witchcraft was generally believed in, and there were laws regarding it. Those suspected were imprisoned, brought to trial and, on conviction, put to death. "Thou shalt not suffer a witch to live" (*Exodus* **22**: 18) is one of the laws of Moses. Jews, Roman Catholics and Protestants tortured, drowned, hanged and burned those suspected of practicing witchcraft.

Two hundred and fifty years ago the Salem witch trials rocked New England. The Scriptures were quoted by Puritan clergymen in support of these trials, just as some clergymen today quote them as an argument against euthanasia. The presiding judge showed no mercy. Two physicians sat on the jury and contributed to the torture of the victims by their cruel tests.[106] Those convicted were hanged. This went on for a year. The turning point came when the citizens of Boston pointed the finger of suspicion at the wife of the Royal Governor. Witchcraft was threatening those on high. The Governor now listened to the more enlightened members of the community. Clergymen, physicians, lawyers and merchants denounced these proceedings as cruel and barbarous, and the witch hunts came to a halt. A wave of repentance swept the populace, and prayers for forgiveness were offered in the churches. Horrible as it all was, the relative abruptness with which the trials stopped and the open repentance of the populace were unique in history. These New Englanders saw to it that this Mosaic law should never again occasion such injustice.

Forty-five years later the following law[107] enacted in the reign of James I was repealed in England:

> All persons invoking any evil spirit, or consulting, coventing with, entertaining, employing, feeding, or rewarding any evil spirit . . . to be used in any witchcraft, sorcery, charm, or enchantment . . . should be guilty of felony without benefit of clergy, and suffer death.

A new law prescribed that "No prosecution shall for the future be carried on against any person for conjuration, witchcraft, sorcery, or enchantment."[107]

The last witch was burned in Spain in 1791 and in Poland in 1793 — a hundred years after the Salem trials.[108] The following quotation from a great scholar on witchcraft is instructive. "No jury, whether in a witch-trial or in any other case, can be more enlightened than the general run of the vicinage."[108] It has been estimated that in England thirty thousand persons suffered death from suspicion of witchcraft during a hundred and fifty years. By rough calculation based on the reports of the last five years there could have been at least an equal number of seriously deformed children born of mothers who had rubella in pregnancy during the past hundred and fifty years in English-speaking countries. New England has shown that, as soon as public opinion becomes sufficiently aroused, it can do away with laws that prove to be unjust. It is to be hoped that in this day and age a change in laws regarding abortion will not have to wait for the virus of rubella to attack the wives of our lawmakers.

Gregg's discovery that rubella early in pregnancy offers great danger of gross deformities in the child represents a distinct advance in medical knowledge. English-speaking countries can take pride in the many painstaking investigations that have enlarged the knowledge on this subject. The cumulated factual evidence presents a challenge to the existing law relative to therapeutic abortion. Although further investigations are needed to determine the accuracy of the evidence, it is certainly sufficient to warrant consideration of another amendment to grant permission for surgical interference after an attack of rubella. Such an amendment can be achieved only through enlightened public opinion.

The argument that the amendment to the law might be abused is, to use the words of the lawyers, "irrelevant, incompetent and immaterial," if untold mental suffering is thereby avoided and more births of healthy infants are achieved.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 33261

PRESENTATION OF CASE

A thirty-year-old man entered the hospital because of convulsive seizures.

He had been well until ten days before admission, when a severe headache had developed. On the next day there was an attack of slight twitching of the right upper lip; shortly afterward the patient became unconscious and had a generalized convulsive seizure. In the next ten hours he had two more attacks, which his wife described as beginning with a twitching of the right corner of the mouth followed rapidly by jerking movements of the right arm and a generalized convulsion. All episodes were preceded by a strange, unpleasant sensation of taste and smell and were followed by transitory nominal aphasia. Three days later the seizures recurred but were limited to the right side of the face and the right arm, without loss of consciousness, and were preceded by an aura of an unpleasant taste and odor. Five days before admission an attack was followed by persistent difficulty in naming objects, clumsiness of the right hand and "numbness" of the right hand and forearm and the right side of the face. The headache recurred intermittently. It was localized to the left temporal region if the patient lay on the left side, but it was severer and more generalized when he lay on the right side. When turning to the left side he felt as though "a bag of water" flowed over to the left side of his head. There had been no visual disturbance, nausea or vomiting.

The past history revealed no serious illnesses. The patient had been in an automobile accident five years previously, with momentary loss of consciousness.

Physical examination revealed a patient who was mentally alert but who had difficulty naming familiar objects. Speech was slurred and hesitant. The visual acuity, visual fields, fundi, pupils and ocular movements were normal. The right hand and arm were weak and clumsy. There were loss of position and gnostic sense in the right hand and a similar although less marked motor and sensory deficit in the right lower extremity. The tongue deviated to the right. The remaining cranial nerves were normal. The arm, knee and ankle jerks were more active on the right than on the left. No pathologic reflexes were elicited.

The temperature, pulse and respirations were normal. The blood pressure was 135 systolic, 90 diastolic.

Examination of the blood showed a hemoglobin of 15 gm. and a white-cell count of 7000. Urinalysis was negative. The initial spinal-fluid pressure was equivalent to 165 mm. of water, with 1 lymphocyte per cubic millimeter and a total protein of 45 mg. per 100 cc. The gold-sol test was negative. X-ray films of the chest were normal. An electroencephalogram showed a "generally rather ragged record, the raggedness most marked at and around the left parietal region." There were no well defined slow waves or indications of a well defined focus.

During the hospital stay, the patient complained occasionally of headache, which was relieved once by lumbar puncture. On the fifth hospital day he had a convulsive seizure involving the face, arm and leg on the right side. Burr holes were made and on the following day a ventriculogram was taken. Only a small quantity of air was visible in the right lateral ventricle, which appeared to be displaced toward the right.

An operation was performed on the sixth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JAMES B. AYER: Three important points are not mentioned in the record. Was there a previous x-ray examination, and what did the plain film show? There is no note of a blood Wassermann or Hinton test. Was the patient right handed? Are the x-ray films of the later examination available?

DR. STANLEY M. WYMAN: These films were made after the burr holes.

DR. AYER: Can any air be seen?

DR. JOST MICHELSEN: This was a difficult ventriculogram. The patient had a seizure during the procedure, and only 8 cc. of air could be injected.

DR. AYER: Is that air in the area of the lateral ventricles?

DR. WYMAN: I cannot be sure.

DR. AYER: Assuming that the report is correct, that the right ventricle has some air in it, the left none, and that the right ventricle is displaced somewhat to the right, let us continue with the analysis. The first thing to ask ourselves is whether the patient had a gross anatomic intracranial lesion, because this must have been an intracranial disturbance. I think that we can say that this is so. The reason I ask that question is that once in a while focal convulsions appear in uremia and other conditions without gross pathologic changes. There

was no history that suggested uremia, and there was a persistence of Jacksonian seizures. I should therefore assume that this patient had an anatomic lesion somewhere within the skull.

What is the localization? The first thing to consider is the localizing symptoms given in the history. There were definitely Jacksonian seizures in the beginning, which frequently went over into general convulsions. These Jacksonian seizures indicate clinically definite localization in the left side of the brain. I think that we can be more accurate and say that the focus was low in the left temporoparietal region, because the lips and the face were first involved. The aura of smell and taste is a definite sign of irritation of the hippocampal region. The headache was primarily on the left side; that is not, of course, a dependable sign for localization, but when it agrees with other things, the headache is often in fairly close proximity to the lesion.

The next symptom to comment on is the aphasia. From the clinical point of view aphasia is a localizing symptom of considerable value. Presumably this man was right handed, and the left side of the brain is therefore indicated. There is no long description of the aphasia, but the record states that it was "nominal." There was also slurring of the speech. That was probably something else and on the motor side of the paresis. Aphasia, primarily nominal, is characteristically seen in lesions of the temporal lobe. There are therefore a good many symptoms and signs on the clinical side alone indicating a lesion that could have been covered roughly by the palm of the hand and was low in the parietal region and primarily motor — although with a sensory overflow after an attack, since it is stated that the patient did not know where things were in his hand, and the aphasia and the aura point to the same region. The lesion may have extended farther, but I prefer to think that the later disturbance was an overflow from pressure or following a seizure and that the lesion itself did not involve the whole parietal region.

The pneumogram is not so conclusive as I thought it would be from the description, but no doubt it is true that there was some displacement of the brain to the right. I do not see how we can escape the conclusion that this was an anatomic lesion of considerable size in the region spoken of and confirmed more or less by the pneumogram. The x-ray films of the skull itself are not mentioned, but I think that they were essentially normal. Is that correct?

DR. MICHELSEN: Yes.

DR. AYER: What are the etiologic possibilities for such an expanding lesion?

The first group of conditions includes tumors, which are the most frequent in such cases. I shall take them up in a moment. The next is an abscess. Could this have been an abscess? That is not a rare cause of these symptoms, with the exception perhaps of the aura of smell and taste, which is unusual in abscess, because probably 9 out of 10 cases come from the ear, which is not mentioned as having been abnormal. There was no discharge from the ear; the patient did not have chronic otitis media. Such abscesses invade the temporal lobe much farther posteriorly and do not give the picture that this patient presented. I am against the diagnosis of abscess because there was no chronic ear condition, because of the presence and importance of the aura of taste and smell and because of the spinal fluid, which showed no cells and which should have shown cells if an abscess had been present. Cysts are rare, especially hydatid cysts. No one has mentioned the liver in this case, and I think that if this had been a cyst the liver would have been enlarged. I have no further comment on cysts.

Granulomas should be considered. The granulomas we have seen have usually been in the upper part of the brain. I do not recall seeing any in this particular location, although I do not know why they should not occur there. The blood Wassermann and Hinton tests are not recorded, but I assume that they were negative. There is nothing in the history and nothing in the examination otherwise to indicate syphilis.

Could this have been a collection of blood? Two types could cause these symptoms. In acute hemorrhage there is sometimes an intracerebral blood clot, which acts in this way. There was nothing in the history to suggest it. There was no blood in the spinal fluid, which there might well have been, and the patient would surely have been sicker than he was, for he was normal between the intervals of convulsions. This I should not expect with an intracerebral collection of blood. The most frequent collection of blood, however, is extracerebral, usually subdural hematoma, which is a bugbear that we often meet. There is a note, which I think is a red herring, that the patient had sustained an injury to the head five years previously; it was apparently not severe but could account for the later development of subdural hematoma. In my experience, however, the mechanism of growth of subdural hematoma should produce these symptoms within a year, usually much sooner, with a lucid interval for months prior to development of symptoms. Five years is long enough to make it most unlikely that subdural hematoma exists. Moreover, these subdural collections are almost always higher in the parietal area. I therefore believe that a subdural collection of blood is unlikely.

The most frequent cause of these expanding lesions is a tumor. There is nothing in favor of metastasis that I can see. Metastatic tumor may be single in the brain but is usually multiple. In a large percentage of cases the lung also shows

metastases. In the case under discussion it failed to do so. The evidence, I believe, points to a single lesion. I see nothing to suggest a lesion elsewhere in the brain or in the nervous system, and I therefore believe that metastasis of any form is not likely. Moreover, the man was only thirty years old, and the usual metastases occur in older people. Two fairly common types of brain tumor that are seen in this location are glioma, which may well give exactly these symptoms, and meningioma. Between the two there is not much to choose. Frequently, meningioma is likely to grow from a petrous ridge or other dural attachment that shows roughening on x-ray study, which is not reported. This is negative evidence that meningioma is less likely and suggests the more probable tumor to be glioma. I should not care to say which type, but evidently it was rapidly growing and that is as far as I dare go.

Could the lesion have been anything else? There is one condition that occurs rarely: blocking of the foramen of Monro, leading to unilateral dilatation of the ventricle, which in turn causes tumor-like symptoms. In this patient an attempt to inject air into the left ventricle seems to have failed, suggesting that it was not enlarged.

I must therefore conclude that we are dealing with an expanding lesion in the left temporoparietal region, not a large one because of the fact that it was not causing an excessive increase in intracranial pressure as judged by the films of the skull, the headache and the spinal-fluid pressure. I should favor an infiltrating glioma. Certainly, a surgical operation is indicated.

DR. CHARLES S. KUBIK: This patient was operated on by Dr. Michelsen, who will describe the pathological findings. But before he does that, are there any suggestions regarding the diagnosis?

DR. JAMES C. WHITE: The only comment I can make is that we have recently been over our brain tumors during the decade 1935–1944, and out of 640 cases in that period 160 patients had seizures, and in those that had seizures astrocytomas were the highest group — 50 per cent of 88 cases. The meningiomas were the second greatest, occurring in 35 per cent. The percentage in the Montreal Neurological Institute is even higher, but in considering Penfield's* series one must remember that anyone who has epilepsy in Canada goes to Montreal. I therefore believe that his statistics of epilepsy associated with brain tumor are overweighted. Two thirds of his patients with supratentorial tumors — and in this hospital, one third — had epilepsy. In glioblastoma multiforme the incidence of seizure is 20 per cent, and in metastatic carcinoma, 14 per cent. In Montreal many patients with astrocytoma and meningioma had epileptic seizures for months or years before operation; in this hospital the duration was only one month. It is also of interest to note that convulsions accompanied many of our brain abscesses.

*Penfield, W., and Erickson, T. C. *Epilepsy and Cerebral Localization: A study of the mechanism, treatment and prevention of epileptic seizures.* 623 pp. Springfield, Illinois: Charles C Thomas, 1941.

CLINICAL DIAGNOSIS

Left frontoparietal brain tumor, probably glioma.

DR. AYER'S DIAGNOSIS

Expanding lesion, left temporoparietal region, probably glioma.

ANATOMICAL DIAGNOSIS

Brain abscess.

PATHOLOGICAL DISCUSSION

DR. MICHELSEN: Our reasoning was very much the same as Dr. Ayer's. First of all, we were not absolutely certain that we were dealing with an expanding lesion. The ventriculogram was done to demonstrate the type of disease. Although the filling was rather poor, we were satisfied, because there was definite displacement of the ventricular system. The location of the lesion was quite obvious clinically. The preoperative diagnosis was brain tumor. We expected a glioma, and because of the rapid course of the disease we thought that this would probably be a glioblastoma multiforme. A bone flap was turned down in the usual fashion. A lesion was readily discovered on the surface, involving the lower portions of the anterior and posterior central gyrus. When we began to take a biopsy, pus escaped from a small opening. On spreading the cortex, a typical abscess wall was found. The pus contained an alpha-hemolytic streptococcus. All of it was evacuated. The dura was closed around the abscess. A catheter drain was put into the cavity and brought out through an opening in the bone flap and scalp. Postoperatively, the patient was treated with penicillin irrigations through the catheter and instillation of penicillin into the subarachnoid space via the lumbar route in addition to intramuscular injections. He has been well since discharge from the hospital. He had some seizures postoperatively and was therefore put on an anticonvulsive regime. Needless to say, this must have been a metastatic abscess. We searched for the primary focus of sepsis, but none was found. We still do not know how this abscess got into the brain.

DR. KUBIK: A small biopsy specimen consisted of brain tissue in which there was infiltration suggesting an acute process with polymorphonuclear leukocytes. There was no fibroblastic capsule.

DR. MICHELSEN: Because of the close proximity to important cortical centers we believed that excision of the capsule would not be advisable at that time.

DR. KUBIK: Occasionally, we see an abscess like this in which no focus of infection can be found. Most cerebral abscesses are a result of sinus infection, otitis media or chronic suppuration in the lungs. We have had two or three fatal cases in which the sinuses, ears and lungs appeared to be normal and in which the source of the infection could not be determined.

DR. WHITE: Has this patient had postoperative seizures? In our experience a great many patients with abscesses have seizures both in the acute stage and after operation.

DR. MICHELSEN: Yes; he had some, but we put him on an anticonvulsion regime, soon after the operation, and I suppose that it worked all right.

DR. AYER: I do not see how the spinal fluid could have been normal. Was it examined carefully?

DR. MICHELSEN: The fluid was examined four times; on one occasion I examined it myself, and only 1 leukocyte per cubic millimeter was found.

DR. AYER: That is unusual in abscess.

DR. MICHELSEN: Of course, the duration was short — only ten days.

DR. AYER: Yes; that often happens in tumor.

DR. KUBIK: In a case of glioblastoma some time ago the entire duration of symptoms was only twelve days. Such a rapid course is rare but does occur occasionally. We have had a few other cases of abscess without cells in the spinal fluid, but those, I believe, were old, chronic abscesses. One would expect cells in an acute case such as this.

CASE 33262

PRESENTATION OF CASE

A seventy-one-year-old Bermudian Negro entered the hospital because of jaundice.

Two and a half years before admission the patient had undergone a combined abdominoperineal resection for an adenocarcinoma (Grade II) of the rectum. On microscopical examination the regional lymph nodes contained no tumor. After operation, the patient was followed in the Out Patient Department periodically for over two years. The colostomy functioned well, and he had no complaints except slight dysuria, narrowing of the urinary stream and dribbling and nocturia. Four months before admission he had a two-week episode of pain in the right flank and pyuria. After catheterization he failed to return to the clinic. Four days before entry the patient's sister noticed that the eyes were yellow. In retrospect he recalled that the urine had left greenish stains on the underclothes for several months. The stools had been lighter than formerly but were still slightly brown or yellow. The appetite was poor, and the patient had been troubled with distention and flatulence after eating. Later he noted that the daily enema returns from the colostomy were delayed over periods of two hours. There had been no abdominal pain, nausea, vomiting or headache. There was no history of itching, bleeding or drug intake.

Physical examination disclosed generalized vitiligo. The pale areas and the scleras were yellow. The liver border extended 6 cm. below the costal margin, the upper limit of dullness being at the fourth rib. Neither the gall bladder nor the spleen could be palpated. The colostomy appeared normal. A rather large, reducible, direct hernia protruded in the left inguinal region. The perineum had healed.

The temperature was 98.8°F., the pulse 70, and the respirations 20. The blood pressure was 120 systolic, 85 diastolic.

Examination of the blood revealed a hemoglobin of 13 gm. and a white-cell count of 15,000, with 72 per cent neutrophils. The urine gave a +++ test for bile and a ++ test for albumin, and the sediment contained 50 white cells per high-power field. The stools were chalk white and semiformed. The van den Bergh reaction was 16.8 mg. per 100 cc. direct, and 24.8 mg. indirect. The cholesterol was 403, the phosphorus 2.8, the nonprotein nitrogen 36 and the calcium 8.0 mg. per 100 cc. The alkaline phosphatase was 70 units per 100 cc. The total protein was 5.3 gm. per 100 cc., with 3.1 gm. of albumin and 2.2 gm. of globulin. The prothrombin time was 25 seconds (normal, 17 to 19 seconds).

X-ray films of the chest were normal. In a gastrointestinal series the duodenal cap appeared markedly narrowed at the tips. There was a slight pressure defect at the point where the superior mesenteric vessels crossed the duodenum, but no definite mass was visualized.

In the hospital the patient's condition remained about the same, although the jaundice increased slightly. Filiform catheters were passed through an obstructed prostatic urethra with difficulty, and constant drainage was instituted. He continued to have crampy postprandial distention, and it took two hours for the daily enema to return. A barium enema passed through the colon into the terminal ileum without evidence of obstruction. A loop of ileum descended into the left inguinal region. Above and medial to this loop was a defect caused by pressure of a soft-tissue mass that was not clearly visualized and lay in the region of the prostate or of the previous operative site in the area of the rectum. This mass measured approximately 7 cm. in diameter.

An operation was performed on the thirteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. DANIEL S. ELLIS: In summary, this patient had undergone an abdominoperineal resection for adenocarcinoma of the rectum two and a half years before admission. He had been well until four months before admission, when urinary symptoms

developed. These had been relieved, and he was again well until four days before admission, when he noted the onset of jaundice. The important physical findings were that the patient was jaundiced and that he had a large liver.

It would be helpful to know what the region of the prostate felt like, but the previous operative procedure made this impossible. The problem resolves itself into the differentiation of the causes of jaundice and we turn to the laboratory for aid. A white-cell count of 15,000 is reported. This is consistent with the finding in obstructive jaundice or intrahepatic disease with considerable destruction of parenchymal tissue. The findings of bile in the urine and chalk-white stools, together with a blood cholesterol of 403 mg. and an alkaline phosphatase of 70 units per 100 cc., point to an obstructive jaundice. The alkaline phosphatase is usually elevated in obstructive jaundice and is not generally high in cases of intrahepatic liver disease without an obstructive component. On the other hand the highest phosphatase I have ever seen was in a patient with biliary cirrhosis, in whom no definite obstruction had ever been demonstrated.

The urinary symptoms and findings were obviously due to an obstruction in the urinary tract, with superimposed infection. From the evidence at hand this obstruction was at the base of the bladder and the region of the prostate, possibly involving the right ureteral orifice.

The x-ray films provide little definite information. The upper gastrointestinal tract appears to have been essentially normal except for some deformity of the duodenal cap, which may or may not represent an old ulcer. I do not see anything in the region of the head of the pancreas. The mass described in the lower abdomen is in the region of the bladder. This could be due to a bladder full of urine, and I should like to know whether or not the clamp that is visible in the region of the catheter was attached to the catheter or not. I am inclined to believe that the mass represents something more than a full bladder because of the previously mentioned urinary symptoms and findings.

If the report of the physical examination is correct, this man had a tremendously large liver, and on this basis alone one suspects something more than primary parenchymal disease in that organ. In discussing the possibilities I think that it might be said that although biliary cirrhosis cannot be ruled out, it is not likely if the findings of a mass in the lower abdomen and the urinary symptoms are to be fitted into the same diagnosis. In any event one possibility is biliary cirrhosis and benign prostatic hypertrophy, with hydronephrosis on the right and superimposed pyelonephritis. A second, likelier diagnosis is a malignant tumor, such as carcinoma of the bladder, with metastases to the liver and to the extrahepatic biliary tract. A third possibility is that this patient had metastases from the original lesion into the lymph nodes in the region of the base of the bladder, causing bladder-neck obstruction and obstruction in the region of the right ureter, and also metastatic spread to the liver. Metastasis to the liver from primary carcinoma of the rectum is usually a late manifestation, although it can occur early. If this patient were from Egypt rather than Bermuda one would have to consider *Schistosoma haematobium* as a cause of cancer of the bladder, with metastatic spread to the liver. This, however, is extremely unlikely. The vague digestive disturbances such as postprandial distention are, I think, perfectly consistent with the degree of liver involvement. The fact, which is mentioned twice, that there was some delay in recurrence from the colostomy enemas does not impress me in view of the negative examination after a barium enema.

In conclusion, I believe that this patient had a malignant tumor with metastases to the liver. I believe that the jaundice was partially due to obstruction of the major radicles of the biliary tree by metastases. This may have been at the porta hepatis, or it may have involved the common duct. The size of the liver suggests that it was full of metastases, and there may have been enough obstruction of the bile canaliculi due to metastases to cause the jaundice. I should not expect white stools however, unless there was obstruction of the hepatic or common bile duct. I suppose that primary carcinoma of the liver could have been present, with the urinary findings on an entirely separate basis. I do not understand why this case is being discussed here today if this were a simple case of metastases to the pelvic floor and to the liver from the original adenocarcinoma. Therefore, I put as my first possibility primary carcinoma of the bladder causing bladder-neck obstruction and interference with drainage of the right ureter, with secondary obstruction in the bladder and kidney and with metastases to the liver and probably elsewhere.

Dr. Benjamin Castleman: The first operation performed at this admission was a peritoneoscopy by Dr. Edward B. Benedict. He found a markedly enlarged liver, whose surface was mottled, grayish green and smooth. No carcinomatous implants were seen. The gall bladder was dilated to three or four times the normal size. The rest of the peritoneal cavity, including the pelvis, was inspected by putting the patient in the Trendelenburg position. A biopsy of the liver was taken.

Have you any comment, Dr. Ellis?

Dr. Ellis: This is further evidence for obstruction of the common duct and against interference with the manufacture and flow of bile into the gall bladder. There may have been a common-duct stone, but there were few symptoms of it other than

jaundice. The large liver still puzzles me, and I think that it was larger than that usually found in biliary cirrhosis. I am probably wrong, but I shall stick to the original diagnosis of metastasis to the liver, with tumor obstructing the common duct. In the absence of positive peritoneoscopic findings of tumor in the pelvis the chances favor metastases from the original carcinoma of the rectum, even after two and a half years.

DR. WADE VOLWILER: I saw this patient after the peritoneoscopy and believed that the distended gall bladder, the elevated cholesterol, the high alkaline phosphatase and the absence of splenomegaly indicated common-duct obstruction by tumor. My best bet was lymph-node metastases from the carcinoma of the rectum. I also believed that there were hepatic metastases not visible by peritoneoscopy.

CLINICAL DIAGNOSIS

Carcinoma of head of pancreas.

DR. ELLIS'S DIAGNOSIS

Metastatic carcinoma of liver and lymph nodes around extrahepatic biliary ducts from carcinoma of bladder or from carcinoma of rectum.

ANATOMICAL DIAGNOSIS

Metastatic adenocarcinoma of lymph nodes around bile ducts from previously resected adenocarcinoma of rectum.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The liver biopsy showed an extreme grade of bile stasis and obstructive cirrhosis, but no evidence of carcinoma.

Following this report the patient was explored with a preoperative diagnosis of carcinoma of the head of the pancreas, this diagnosis being chosen probably because of the slight pressure on the duodenum visualized on the x-ray films. At operation the liver was large and slightly granular but showed no evidence of carcinoma. The gall bladder was tremendously dilated, measuring about 10 cm. in diameter. Surrounding and compressing the extrahepatic bile ducts were nodules of tumor that proved microscopically to be adenocarcinoma characteristic of the type seen in the colon.

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THE BOSTON DISPENSARY

The Boston Dispensary in March of this year, with Surgeon General Parran as guest speaker, celebrated a little tardily its one hundred and fiftieth anniversary. This sesquicentennial celebration — the half century is still an important landmark in our young country — serves to recall certain events in the history of the Dispensary, as well as its present needs.

The Dispensary, we are reminded, came officially into being at the Boston Chamber of Commerce on September 11, 1796, with the acceptance by a group of citizens of a report from Dr. Oliver Smith and Mr. William Tudor providing rules and regulations for the proposed institution. The third such dispensary in the country and today the only survivor of the three, the Boston Dispensary was also the first medical charity in New England.

Coming into existence less than twenty years after the signing of the Declaration of Independence, the Dispensary followed by fifteen years the foundation of the Massachusetts Medical Society — the first state society in the country with a continuous existence — and antedated by sixteen years the establishment of the *New England Journal of Medicine and Surgery* and by twenty-five years the opening of the doors of the Massachusetts General Hospital.

Thomas Bartlett's apothecary shop on Corn Hill became the first headquarters of the organization and here hung its first signboard, bearing the picture of the Good Samaritan to represent its functions. Its three main principles were embodied in the report submitted by Dr. Smith and Mr. Tudor:

> **The sick, without being pained by a separation from their families, may be attended and relieved in their own houses.**
>
> **The sick can, in this way, be assisted at a less expense to the public than in any hospital.**
>
> **Those who have seen better days may be comforted without being humiliated; and all the poor receive the benefits of a charity, the more refined as it is the more secret.**

The services of the Dispensary increased as the town and the Commonwealth prospered. In 1801 it was incorporated; twenty years later, on the principle that "the moral effect of a clean skin is often more potent in the treatment of ailments than the administration of drugs," it procured a bathtub to be located conveniently "in some central place." In 1856 its clinic for ambulatory patients was opened, in 1873 the country's first clinic for syphilis and the first dental clinic, and in 1899 the first pulmonary clinic.

The Boston Floating Hospital, finally grounded, was established on land in conjunction with the Dispensary in 1929, and at the time of this union plans for the New England Medical Center, to include Tufts College Medical and Dental schools were formed. The Joseph H. Pratt Diagnostic Hospital was added in 1938.

Like all the charitable institutions that have carried on through the war years without expansion, the Dispensary is now in need of funds to

continue the fulfillment of its destiny. Other charities may have an equal claim on the generosity of the public; surely none can have a greater.

REFSUM'S DISEASE

A FAMILIAL disease, not hitherto described, has recently been reported from Norway.* The syndrome was observed in two Norwegian families, not related to each other. In one, a brother and a sister were affected; in the other, two sisters and their cousin. The chief symptoms were hemeralopia (retinitis pigmentosa), polyneuritis, ataxia and other cerebellar manifestations. Both patients in the first family died suddenly of respiratory paralysis. The pathologic changes were limited to the brain, with degeneration in the lipoid content and pigment anomalies. The lesions closely resembled those found in Niemann–Pick disease and in familial amaurotic idiocy.

The first clinical symptoms were limitation of the fields of vision and hemeralopia. These complaints often preceded difficulty in walking, due to the ataxia, by many years. Paresthesias were most marked in the hands and feet. In some cases the pain was said to be "burning" or "shooting" in character. No case showed mental manifestations. The ataxia was of the cerebellar type, and other vague cerebellar symptoms were occasionally present. The cerebrospinal fluids contained large amounts of protein, without a corresponding increase in cells, findings somewhat similar to those in the Guillain–Barré syndrome. Three patients had sinus tachycardia by electrocardiographic examination. Others had abnormalities of the pupils, deafness or epiphyseal dysplasia. The syndrome was considered hereditary, probably of a simple recessive type. When large amounts of vitamins were given, at least one patient showed objective improvement.

*Refsum, Sigvald. *Heredopathia Atactica Polyneuritiformis.* 303 pp. Oslo: J. G. Tanum, 1946.

MASSACHUSETTS MEDICAL SOCIETY

ANNUAL REGISTRATION IN INDIANA

Indiana has recently passed a law requiring annual registration of physicians, which becomes effective on July 1. The fee for those who are nonresidents is $10.00, and the licensee must register before August 31. Since failure to register results in automatic cancellation of the certificate, all who hold Indiana licenses and wish to retain them should obtain an application for registration from the State Board of Medical Registration and Examination, 416 K. of P. Building, Indianapolis 4.

JOSEPH GARLAND, *Secretary*

ANNUAL GOLF TOURNAMENT

The winners at the annual golf tournament of the Massachusetts Medical Society, which was held at the Woodland Golf Club on the afternoon of May 20, were as follows: low gross, R. J. Nugent; second low gross, M. Sargent; low net, A. D. Crowell; and second low net, G. Quigley.

MISCELLANY

NOTE

Dr. Duncan E. Reid will become William Lambert Richardson Professor of Obstetrics at the Harvard Medical School and obstetrician-in-chief to the Boston Lying-in Hospital on July 1. He succeeds Dr. Frederick C. Irving, who resigned both positions as of December 31, 1946. Dr. Reid has served continuously on the staff of the Lying-in Hospital since 1933, and joined the staff of the Harvard Medical School in 1935. Born in Burr Oak, Iowa, on December 22, 1905, he graduated from Ripon College in 1927. He received his medical degree from Northwestern University in 1932 and served as an intern and resident at the Passavant Memorial and St. Luke's hospitals of that city before coming to Boston.

CORRESPONDENCE

LABORATORY TRAINING IN PARASITOLOGY

To the Editor: The *Journal* is to be congratulated on the excellent editorial, "Diagnosis of Amebiasis by Stool Examination," that appeared in the April 24 issue. It demonstrates a thorough understanding of the laboratory problems involved in this difficult examination. It agrees closely with what we believe and teach in the Parasitology Branch of the Laboratory Division of the Public Health Service. Since the editorial mentions "the need for improved training of hospital laboratory technicians in the performance of stool examinations," you may be interested in knowing about our laboratory training program.

Since October, 1945, we have been conducting a six weeks' course in the laboratory diagnosis of parasitic diseases, seven sessions having been completed. This course is open to all grades of laboratory personnel, and although at the present time our first responsibility is to the laboratories of state and local health departments, we are glad to accept persons from private hospitals and laboratories as vacancies occur. There is no tuition or laboratory fee, but travel and living expenses must be paid for by the individual or his employer.

In addition to the parasitology course, the Laboratory Division offers an extension service of parasitologic materials. This service involves monthly shipments of specimens that are numbered and accompanied by a key to the correct diagnosis. This service is also open to state and local health departments and to the students who have attended our course in Atlanta.

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(*Notices on page xix*)